Palladium- and Ruthenium-Catalyzed Decarboxylative Allylations and Michael Addition-Allylation Reactions. Applications in Nitrogen Heterocycle Synthesis

By

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Abstract

Chao Wang, Ph.D.

Department of Chemistry, June 2008

University of Kansas

Our group has a long-standing interest in Pd or Ru-catalyzed decarboxylative coupling reactions. It has been shown that allyl β-ketoesters, upon treatment with palladium or ruthenium, generate freely diffusing enolates and π-allyl electrophiles. Consequently, we were curious about whether appropriate reactants (such as Michael acceptors) could be used to intercept these intermediates during the reaction. It has been since shown that a $[Cp^*RuCl]_4$/bipyridyl catalyst effectively induces a regioselective tandem Michael addition-allylation reaction. This protocol works well with a variety of allyl β-ketoesters and Michael acceptors. Interestingly, ruthenium complexes behave as bifunctional catalysts, which activate the electrophilic allyl fragment and catalyze the decarboxylative formation of enolate nucleophiles. In addition, we have shown that cyclic carbamates diastereoselectively produce vinyl azetidines in good yields via a decarboxylative ring contraction. The diastereoselectivity is facilitated by rapid epimerization of the C_5 stereocenter through π-σ-π allyl interconversion. This allows the synthesis of highly diastereoenriched azetidines from diastereomeric mixtures of cyclic allylic carbamates. Furthermore, in

the presence of Michael acceptors, the cyclic carbamates undergo tandem Michael addition-allylation to produce highly substituted piperidines with good diastereoselectivity. Moreover, we have demonstrated that vinyl benzoxazinones undergo decarboxylative allylation to generate a series of dihydroquinoline derivatives. Once again, reaction in the presence of Michael acceptors led to a formal decarboxylative [4+2] cycloaddition. The analogous reaction in the presence of nonracemic palladium catalysts led to a highly enantioselective reaction. Lastly, a selenium-catalyzed oxidative halogenation of carbonyl compounds was developed. Interestingly, phenylselenides were found to be efficient and selective catalysts that enhance the electrophilicity of oxidized halogen sources such as NCS toward α–halogenation of carbonyl containing compounds such as ketones, β-ketoesters, and even α,β-unsaturated ketones. In most cases, monohalogenated products were generated exclusively.

To my wife, Lisha

and my baby, Gavin

Acknowledgement

Five years of graduate study is not that easy, which were composed with both joys and tears. When I looked back, there are so many peoples I have been worked with, and without their help, I can never stick to my graduate study and summit such a big mountain in my life. So I feel like to say something and express my great appreciation of their companionship.

I want to say “thank you” to my wife, Lisha. You always believe in me and have been supportive during my graduate study. Even though we are different in majors, you are willing to talk about chemistry and apparently chemistry is not your favorite spot. I still remembered those times you had to listen to my practice talks and provide me with valuable feedbacks. In living, I really enjoyed your company, which makes things easier. Though you seldom cook, I must admit that I did enjoy cooking. You are an extremely smart, smart PhD candidate and just need a little bit more focus. My baby-Gavin is really a blessing to us. I just can not imagine you are almost two years old now. To watch you growing up make me happy everyday. Being a daddy is not only changing dippers, feeding, but to spend a lot of time together and have fun. I love you both very much.

To Jon, you are a very nice and acknowledge advisor. Sometimes I just curious where did you learn all those chemistry. You are a hardworking “boss” with so many smart ideas. I could not have asked for a better PhD mentor. I know it must be very hard to guide me through my graduate study since my native language is not English. I remembered those times we sat together, going though my slides, my drafts and more importantly, my dissertation. I just can not imagine that you actually went through my dissertation four times. As to your personality, you have always been very nice and considerate. More importantly, you treat every lab members in a fair manner. Your inquisitiveness and curiosity about science impressed me the most and will

impact my whole life. You do set up a model for me to follow in the future.

I also want to express my gratitude to other committee members, Dr Carlson, Helena, Jeff and Paul. You taught me that there are a lot of funs in chemistry, which made my journey to my PhD degree more pleasant. I really appreciate your mentorship. Dr Carlson, you are my advisor on organic colloquium and taught me the spectroscopy course. I am always impressed at your organization and dedication to your students. Jeff and Paul, your knowledge and provoking points at the problem sets make learning more fun, and I did have a wonderful time at KU. Helena, I sat in your synthesis course and have been working as a GTA with you. Your innovative ways of teaching is awesome. Again, I would like to thank Helena and Paul for being the readers of my dissertation.

To Erin and Shelli and Dr Li, it is lucky to have you as the seniors in the lab. Erin, your attitude and dedication to chemistry impressed me the most. Shelli, without you, the Tunge's lab would not run so smoothly. I did enjoy working with you fellows and truly appreciate your help with my oral proposal. Dr Li, you are the first post-doc I ever worked with. Many thanks for teaching me those experimental "tricks" and discussion chemistry with me in Chinese. I felt sorry for the rest of the members of Tunge's group for suffering those blablabla…; however it does show that "learning a second language is important".

I also want to thank other members of Tunge's group. Jimmie Weaver, Robert Torregrosa, Alex Greening, Antonio Recio, Rushi Trivedi, Ranjan Jana, Nirmal Pahadi and Shaofeng Duan. You fellows are great members and I have a good time working with you in the lab. I am expecting to see Tunge's group gets bigger and stronger in the near future.

I also wish to take this chance to express my gratitude to the molecular structure group at KU, Dave Vander Velde and Sarah Neuenswander for NMR sepectroscopy

analysis, Todd Williams and Bob Drake for Mass Spectroscopy analysis and Victor Day for X-ray crystallographic analysis.

Finally, I want to share my joy with my family. I have been very lucky to live with them in the past two years. My parents, Wenzhi Wang and Xuejie Zhang, your encouragement and supportiveness hold me up and help me go through the good times and bad times of my graduate study, and here I become the first member of the family with a PhD degree. My parents-in-law, Ruxing Zhang and Ying Du, You are great and I can not imagine to finish my study here at KU without your help. I enjoy playing games together and I love you all.

Palladium- and Ruthenium-Catalyzed Decarboxylative Tandem Michael Additon-Allylation Reactions and Further Applications in Nitrogen Heterocycles Synthesis

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Abbreviations

Ac	acetyl
Ar	aryl
Bn	benzyl
Bu	butyl
Bz	benzoyl
cat.	catalytic
COD	cyclooctadiene
COT	1,3,5-cyclooctatriene
COSY	correlation spectroscopy
Cp	cyclopentadienyl
dba	dibenzylidene acetone
de	diastereomeric excess
DEPT	distortionless enhancement by polarization transfer
DIEA	diisopropylethylamine
DMA	dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DMF	*N*, *N*-dimethylformamide
DMSO	dimethylsulfoxide
dppb	diphenylphosphinobutane
dppe	diphenylphosphinoethane
dppp	diphenylphosphinopropane
dppf	1,1'-bis(diphenylphosphino)ferrocene
dr	diastereomeric ratio
ee	enantiomeric excess
ent	enantiomer
Et	ethyl

EWG	electron-withdrawing group
GC	gas chromatography
Het	heteroaryl
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrometry
IR	infrared radiation
LAH	lithim aluminum hydride
LDA	lithim diisopropylamide
Ln	ligand
Me	methyl
NBS	*N*-bromosuccinimide
n-BuLi	*n*-butyl lithium
NCS	*N*-chlorosuccinimide
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
Ns	*p*-nitrobenzene sulfonyl
Np	naphthyl
NXS	*N*-halosuccinimide
Nuc	nucleophile
Pd	palladium
Ph	phenyl
ppm	part per million
Se	selenium
sec-BuLi	*sec*-butyl lithium
Succ	succinimide
TBAB	tetrabutylammonium bromide
TBAF	tetrabutylammonium fluoride
^{t}Bu	*tert*-butyl

Tf	triflate
TMEDA	tetramethylethylene diamine
TMG	tetramethylguanidine
TMSCl	trimethylsilyl chloride
tol	toluene
Ts	tosyl
μW	microwave

Chapter 1

Ruthenium-Catalyzed Decarboxylative Insertion of Michael Acceptors into Allyl Ketoesters

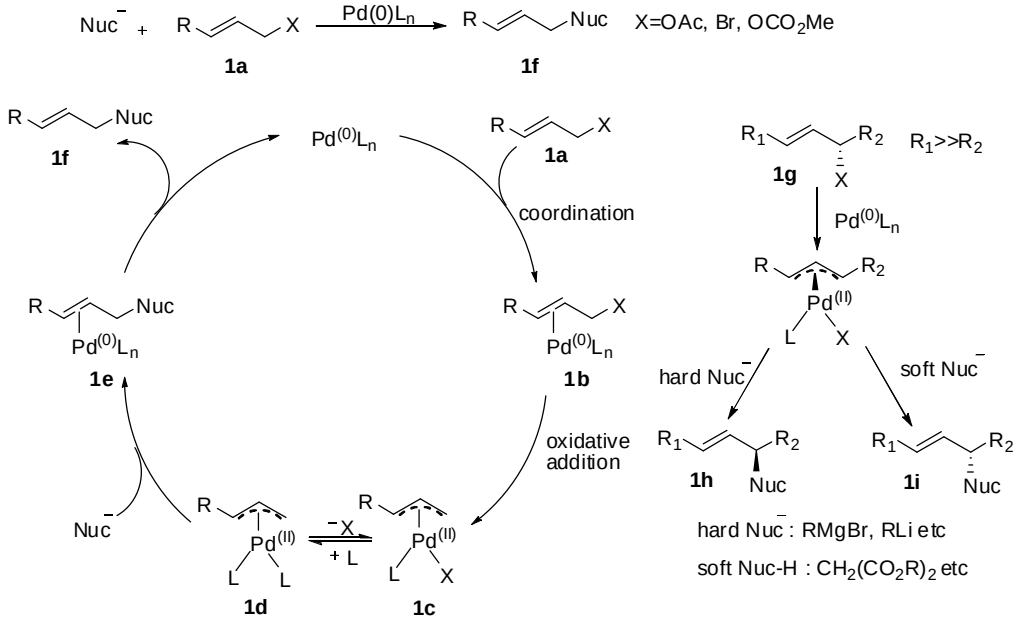
1.1 Overview of Ruthenium-Catalyzed Allylation Reactions

New methodologies for C-C bond formation have been driving progress in synthetic organic chemistry. Transition metals were introduced as reagents and catalysts in this scenario because they often allow reactions to proceed under mild conditions and with high functional group compatibility. Furthermore, transition metal complex-catalyzed reactions are often highly chemoselective, regioelective and stereoselective, so they have found wide applications in modern synthesis.[1] Also of note here is that transition metal functions by either activating the reactants or by stabilizing the high energy transition state and product through coordination.[2]

Palladium and ruthenium-catalyzed allylic alkylations have attracted many research groups' interest across the world. Possibly one of the most remarkable examples is the Tsuji-Trost allylation reaction,[3, 4] which has been extensively explored and generated thousands of references since its discovery in 1965. The general reaction scheme and mechanism are shown in Scheme 1. The reaction starts by coordination of the Pd(0) catalyst to the allylic substrate **1a**, followed by nucleophilic displacement of the leaving group to generate a π-allylpalladium complex **1c**, which undergoes nucleophilic substitution to generate the allylation product **1f**. Trost proposed two different mechanisms, depending on the nature of the nucleophiles.[5] With hard nucleophiles, the reaction was thought to proceed by ligand exchanging

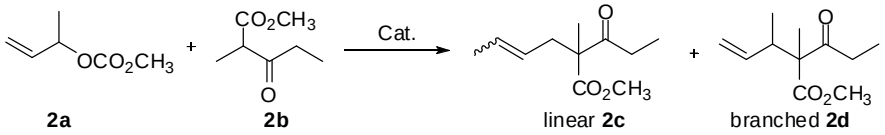
first, followed by reductive elimination to give the product **1h** with reversed stereochemistry; while the soft nucleophiles attack the π-allyl unit directly in the sense of S_N2 reaction, during which double inversion generates the product **1i** with overall retention stereochemistry.

Scheme 1 *Tsuji-Trost allylation reaction*



Palladium-catalyzed allylic alkylations normally generate linear products as compared to ruthenium catalysts, which afford branched products.[5] Tsuji reported the first ruthenium catalyzed allylic alkylation in 1985 as illustrated in Scheme 2.[6] The combination of $RhH(PPh_3)_4$ with *n*-butyl phosphine favored the branched product **2d**, while the palladium catalyst generated a mixture of linear **2c** and branched product **2d** in a ratio of 73:27.

Scheme 2 *Ruthenium-catalyzed regioselctive allylation*

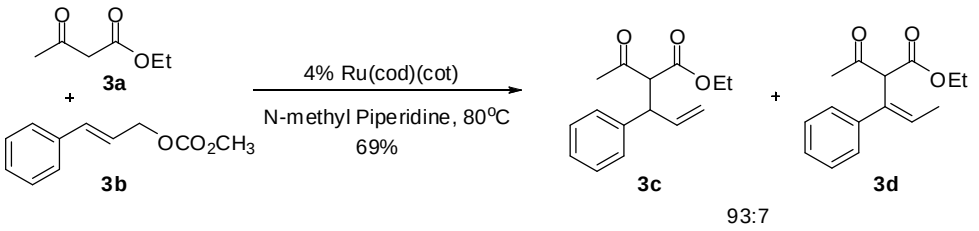


2a **2b** linear **2c** branched **2d**

Cat	Yield	Ratio **2c:2d**
$Pd_2(dba)_3/PPh_3$	89	73:27
$RhH(PPh_3)_4/P^nBu_3$	81	14:86
$RuH_2(PPh_3)_4$	61	32:68

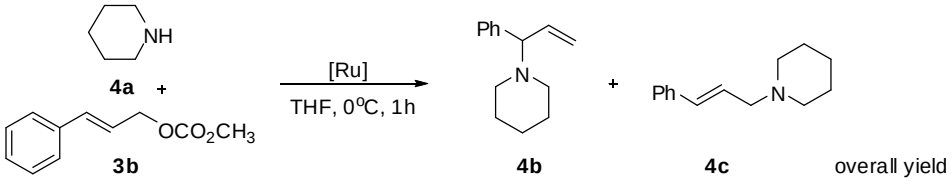
Much early work in the field of ruthenium-catalyzed allylic alkylations was done by Watanabe et al. In 1993, Watanabe published their results on different ruthenium complex-catalyzed allylations of β-ketoesters with allylic carbonates (Scheme 3).[7] A Ru(COD)(COT) complex was found to favor the addition of nucleophiles to the more substituted terminus of the Ru-allyl complex as shown in Scheme 3. The addition of ethyl acetoacetate **3a** to cinnamyl methyl carbonate **3b** is quite regioselective, affording exclusively the branched product. Also included are other ruthenium complexes, such as $Ru_3(CO)_3$, $RuH_2(PPh_3)_4$, $RuCl_2((PPh_3)_2$ and $RuCl_3$; however those catalysts showed little or no reactivity toward allylation reaction. It was proposed that the regioselectivity depends on the structure of the substrates and ligands that coordinate to the ruthenium catalyst. For instance, the ratio of linear to branched product dropped to 50:50 when dimethyl or diethyl malonate were used as nuceleophiles instead of the ketoester.

Scheme 3 *Ru(COD)(COT) catalyzed regioselctive allylation of β-ketoesters*



Along this line, various Ru(II) catalysts were developed in order to incorporate heteroatom nucleophiles rather than carbon nucleophiles. For example, $Cp^*RuCl(cod)$ was found to catalyze allylic amination of cinnamyl methyl carbonate **3b**, which generated the branched product **4b** and linear product **4c** in a ratio of 84:16 (Scheme 4).[8]

Scheme 4 *[$Cp^*RuCl(cod)$] catalyzed allylic amination*

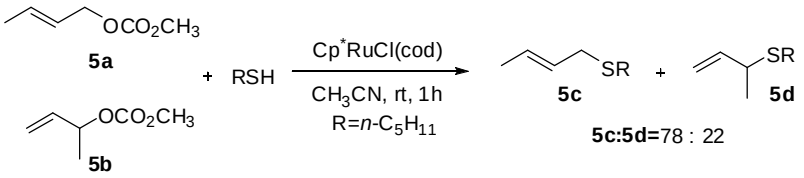


	4b		4c	overall yield
[Ru]= $Cp^*RuCl(cod)$	84	:	16	99%
$Cp^*RuBr(cod)$	84	:	16	99%
$[Cp^*RuOMe]_2$	83	:	17	99%
$[Cp^*RuCl_2]_2$	83	:	17	99%

In 1999, the same $Cp^*RuCl(cod)$ catalyst was used for the allylation of thiols,[9] which were generally thought to poison transition metal catalysts due to their strong coordinating ability.[10] This reaction was relatively regioselective and favored the linear allylic thioether (Scheme 5). Interestingly, under mild reaction conditions, two

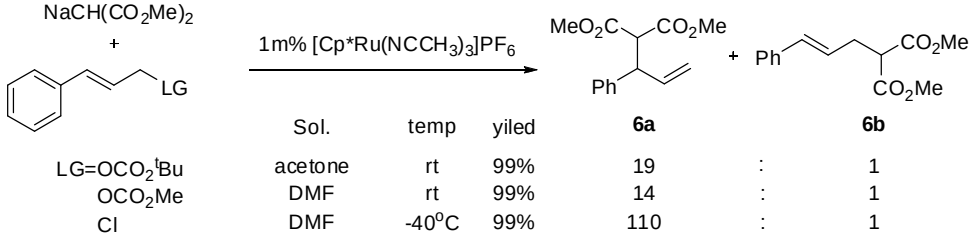
regioisomers **5a** and **5b** gave an identical mixture of products **5c** and **5d** in a ratio of 78:22 and 95% and 77% yield respectivly. Thus, it was logically proposed that a π-allylruthenium complex was involved as the reactive intermediate. [$CpRu(PPh_3)_2Cl$] was also shown to catalyze allylation of phenols and thiols, however the regioselectivity was only 50:50.[11]

Scheme 5 *Regioselective thiol allylation*



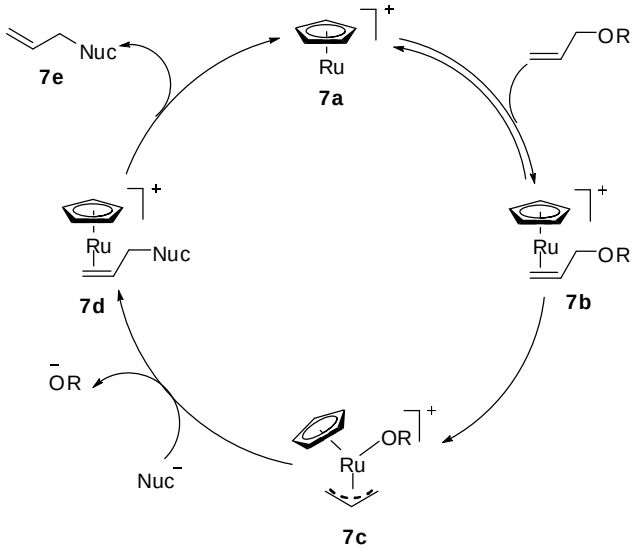
In 2002, Trost reported a stereospecific allylic alkylation with [$Cp^*Ru(NCCH_3)_3$]PF_6.[12] This Ru-catalyzed allylation proved to be highly regioselective, favoring the branched product **6a** over linear product **6b** as illustrated in Scheme 6. The reaction conditions were generally mild, however a general solvent and temperature that was effective for all substrates was not found.

Scheme 6 *[$Cp^*Ru(NCCH_3)_3$]PF_6- catalyzed regioselecitive allylation*



The general reaction mechanism is thought to proceed by formation of ruthenium π-allyl complex **7c**, followed by nucleophilic attack at the more substituted allyl terminus to generate **7d**. Decomplexation then produces allylic alkylation product **7e** and regenerates the catalyst **7a**.[13]

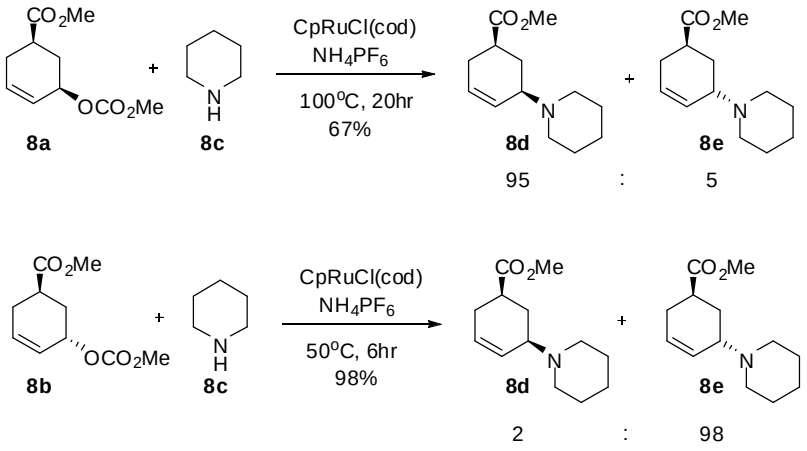
Scheme 7 *Proposed catalytic cycle*



To investigate the stereochemical course of the Ru-catalyzed allylation, two diastereoisomers **8a** and **8b** were synthesized and allowed to react with piperidine **8c** in the presence of 5 mol% of [CpRuCl(cod)] and 5 mol% of NH_4PF_6.[14] The *cis*-carbonate **8a** gave primarily *cis*-product **8d**; whereas in the case of *trans*-carbonate **8b**, *trans*-product **8e** was produced predominately over **8d** in a ratio of 98:2. This result indicates a double inversion mechanism giving rise to overall retention of stereochemistry, which is consistent with the stereochemical course of

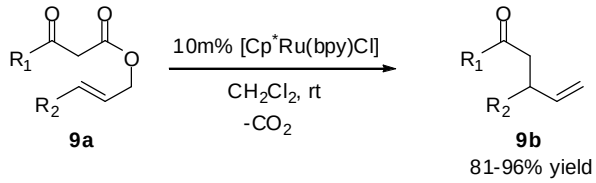
related Pd-catalyzed allylic substitutions.[15]

Scheme 8 *Stereochemical course of Ru-catalyzed allylation*



Our research group has been interested in extending the utility of the above transformations to the use of ketone enolates using transition metal-catalyzed decarboxylative allylation. For instance, Erin showed that allyl β-ketoesters **9a** combined with a [Cp*Ru(bpy)Cl] catalyst undergo regioselective allylation to form γ,δ-unsaturated ketones **9b** under neutral conditions (Scheme 9).[16] To be noted here is that non-stabilized ketone enolates were formed under extremely mild reaction conditions compared to the traditional methods of generating ketone enolates using strong bases such as lithium diisopropylamide. As expected, Ru-catalyzed allylic alkylation favors the branched products **9b**, and in most cases, the regioselectivity was over 19:1.

Scheme 9 *Synthesis of γ,δ-unsaturated ketones from allyl β-ketoesters*



1.2 Palladium-Catalyzed Decarboxylative Generation of Enolate Nucleophiles

1.2.1 Palladium-Catalyzed Decarboxylative Generation of Enolate Nucleophiles

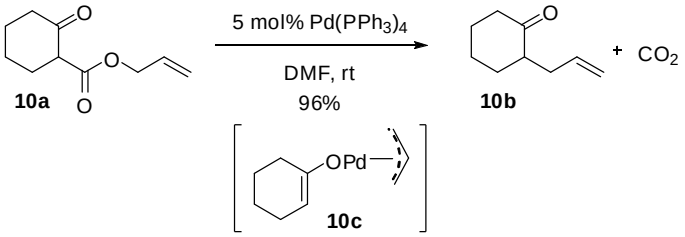
The concept of differing reactivity of "hard" and "soft" nucleophiles with palladium π-allyl complexes was introduced in 1996 by Trost et al.[5] "Soft" nucleophiles refer to those resulting from conjugated acids with a pK_a less than 25; whereas "hard" nucleophiles are defined as those, whose conjugated acids have a pK_a that is greater than 25. Those nucleophiles are also called non-stabilized nucleophiles. The two types of nucleophiles react differently with non-stabilized nucleophiles coordinating to the metals before nucleophilic attack, while stabilized nucleophiles attack the π-allyl species directly.

Allylation of non-stabilized nucleophiles, for example ketone enolates, was traditionally carried out in the presence of a strong base, which limits its synthetic utility if the substrate contains base-labile functional groups or multiple enolizable hydrogens. As such, methodology performed under non-basic conditions would be highly desirable. Interestingly, allyl β-ketoesters, upon treatment with palladium

generate ketone enolates under extremely mild conditions. Pioneering work in this field was done by Tsuji and Saegusa.[17-20]

In 1980, Saegusa reported a facile Pd-catalyzed decarboxylative allylation with allyl cyclohexanone-2-carboxylate **10a** as shown in Scheme 10.[17] A Pd(II) enolate intermediate **10c** was thought to be involved in the course of this reaction.

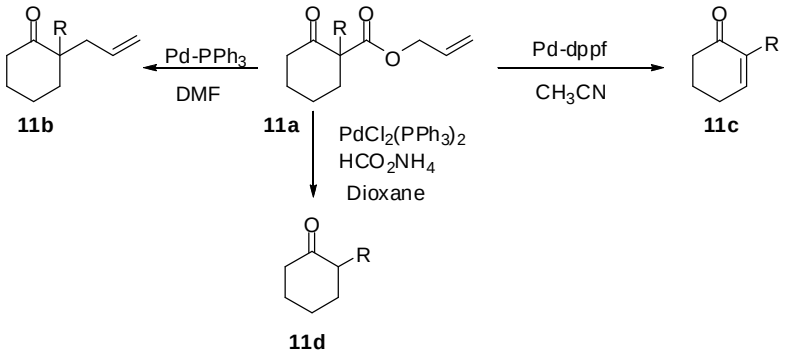
Scheme 10 *Pd-catalyzed decarboxylative allylation with cyclic allyl β-ketoesters*



Following that, Tsuji further investigated the ligand effects and reported a Pd-catalyzed decarboxylation-dehydrogenation to produce various α,β-unsaturated ketones **11c** (Scheme 11).[18] A bidentate phosphine ligand, diphenylphosphino ferrocene (dppf), combined with a Pd catalyst precursor produced mainly enone products **11c** in refluxing acetonitrile. In contrast, triphenylphosphine ligand gave the decarboxylative allylation product **11b**. Protonated product **11d** was formed in the presence of ammonium formate, which further enriched the synthetic utility of allyl β-ketoesters. Noteworthy is that solvents also play a key role here and it has been shown that aprotic solvents such as DMF and acetonitrile favor the formation of enones. On the other hand, allylation occurred in *t*-butyl alcohol. Interestingly, the

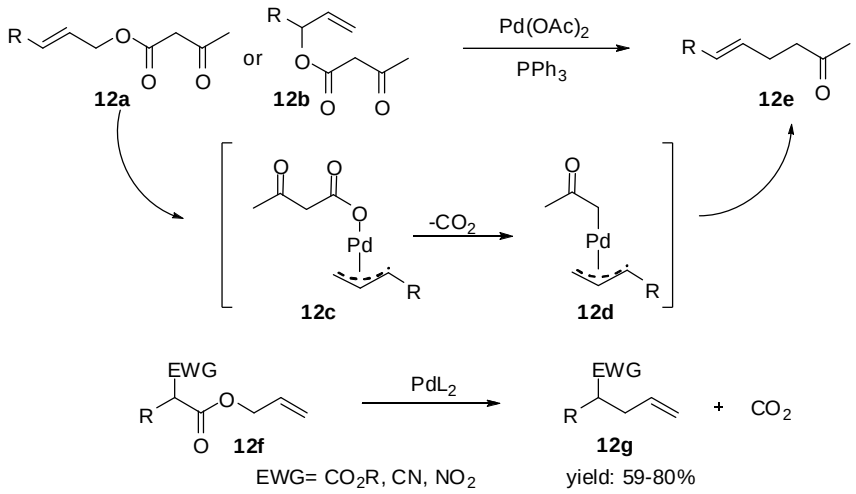
presence of an α-substituent R is crucial for the formation of **11c**. For example, allylation product **11b** was formed in almost equal amount as well as double allylation products when R equals to hydrogen.

Scheme 11 *Pd-catalyzed decarboxylation-dehydrogenation*



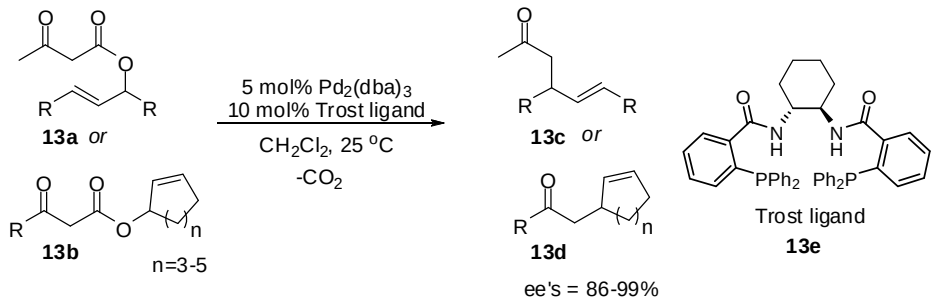
Furthermore, acyclic allyl β-ketoesters **12a** have been shown to undergo a regioselective decarboxylative allylation smoothly, producing the γ,δ-unsaturated ketone products **12e** through nucleophilic attack at the less substituted terminus of the Pd-allyl complex **12d** (Scheme 12).[19] Also of note is that regioisomeric reactant, **12b**, gave the identical linear olefin products **12e** as expected for a reaction involving a π-allylpalladium intermediate **12d**.

Scheme 12 *Acyclic substrates for decarboxylative allylation*



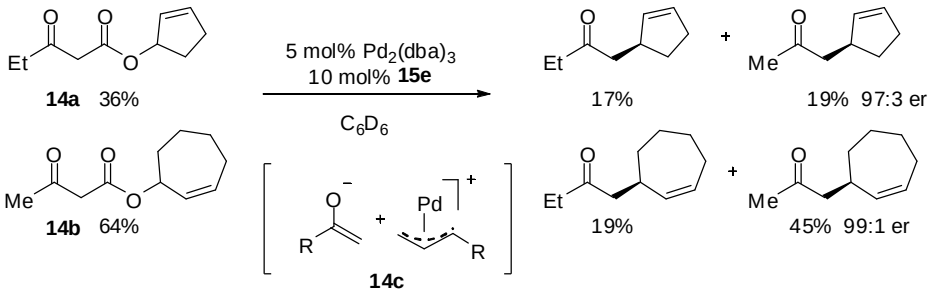
In addition to ketoesters, starting materials with other electron-withdrawing groups (EWG), such as ester, nitrile, and nitro were also investigated (Scheme 12),[20] however, malonate and cyanoacetate substrates were somewhat less reactive than the corresponding carbonyl substrates **12a**, and consequently higher temperatures were required. For instance, when the EWG was CO_2Me, decarboxylative allylation was carried out in refluxing dioxane or DMF, affording product **12g** in 75% yield.

Scheme 13 *Asymmetric allylic alkylation (AAA)*



In 2004, Burger and Tunge reported an asymmetric allylic alkylation (AAA) of non-stabilized ketone enolates catalyzed by a combination of 5 mol% $Pd_2(dba)_3$ and 10 mol% Trost ligand **13e** as illustrated in Scheme 13.[21] The allylation products **13c** and **13d** were obtained in excellent enantioselectivity. Also included in this report was a crossover experiment, conducted to investigate whether the decarboxylative allylation occurred intra- or intermolecularly (Scheme 14). Treatment of a mixture of substrates **14a** and **14b** with the standard reaction conditions afforded almost equal quantities of all four possible products. This result seems to indicate that freely diffusing enolates (or enolate precursors) and π-allylpalladium species **14c** were generated during the course of the reaction. This phenomenon was also noted by others, consequently intramolecular trapping of the generated enolates with aldehydes was reported.[22]

Scheme 14 *Crossover experiment*

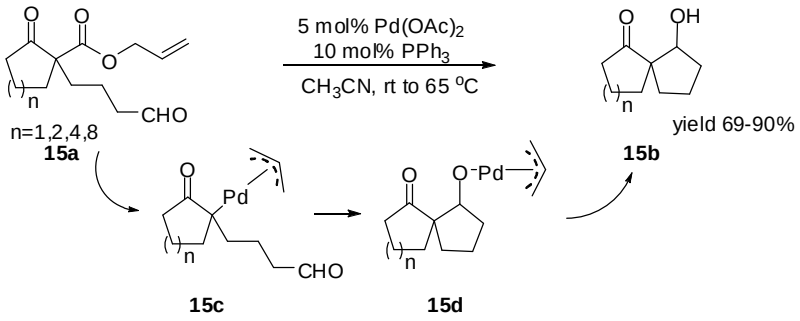


1.2.2 Multiple Transformations Via Palladium Enolate Chemistry

Palladium enolates have been postulated as important intermediates in the

decarboxylative allylic alkylation of β-ketoesters (Scheme 15).[17] In their subsequent study, Tsuji reported the first intramolecular aldol reaction of palladium enolates with aldehydes under non-basic conditions.[22] Oxidative addition of allyl β-ketoesters **15a** to Pd(0), followed by decarboxylation generated a Pd(II) enolate **15c**, which underwent an intramolecular aldol reaction to smoothly produce **15d**. Aldol products **15b** were obtained in good to excellent yield. The regeneration of the palladium catalyst from intermediate **15d** was unfortunately not addressed by this report.

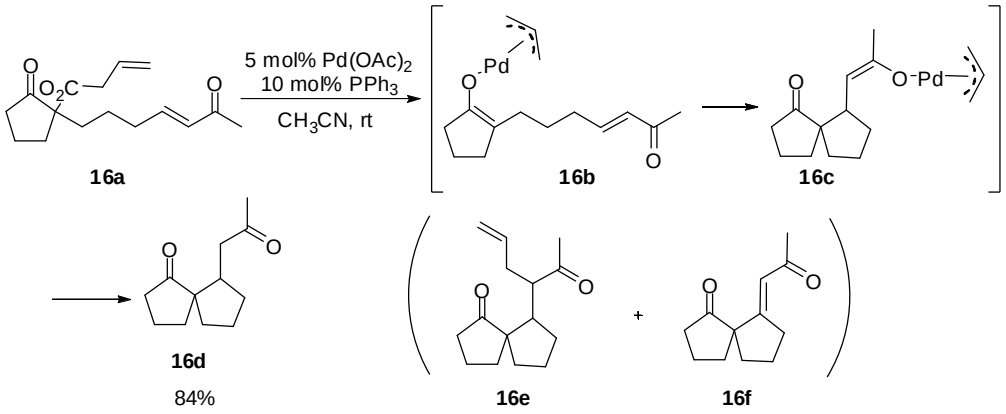
Scheme 15 *Intramolecular aldol reaction with allyl β-ketoesters*



Various α, β-unsaturated ketones tethered to allyl β-ketoesters were also shown to react with palladium enolates, generated by decarboxylation of allyl β-ketoesters to produce cyclic Michael adducts **16d** (Scheme 16).[23] Also included in this report was a brief screening of reaction conditions to optimize the yield of Michael adducts **16d**. It was found that treatment of **16a** with catalytic amount of $Pd(PPh_3)_4$ in CH_3CN at room temperature generated exclusively the Michael product **16d** by protonation of intermediate **16c**, while the Michael addition/allylation product **16e** and the Michael

addition/β-hydride elimination product **16f** were formed as minor products under other conditions. This reaction was proposed to go through a similar pathway as the intramolecular aldol reaction shown in Scheme 15.

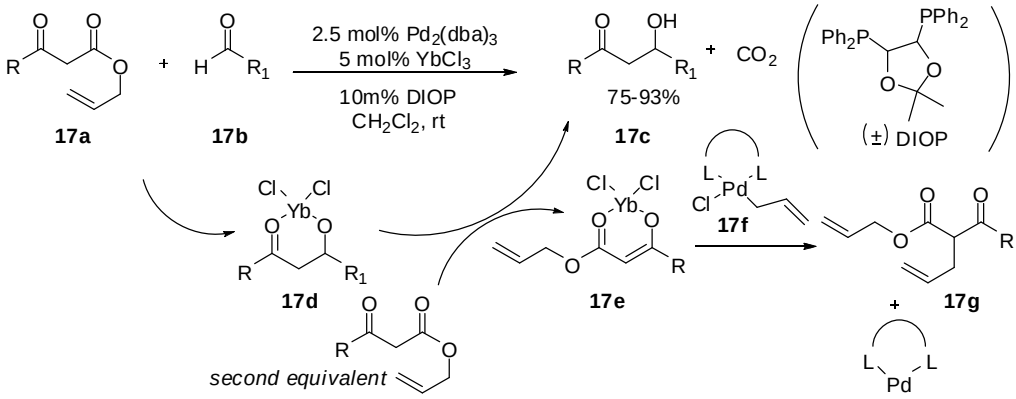
Scheme 16 *Intramolecular Michael Addition with allyl β-ketoesters*



Even though those Pd-enolates have been shown to undergo intramolecular nucleophilic additions to aldehydes and enones, the intermolecular version is problematic due to the competitive decarboxylative allylic alkylations.[24] In this regard, a hetero-bimetallic catalyst complex was shown to efficiently catalyze the intermolecular decarboxylative aldol reaction of allyl β–ketoesters with aldehydes as shown in Scheme 17.[25] The incorporation of a metal salt $YbCl_3$ was thought to promote either the formation of metal enolates or nucleophilic additions by increasing the eletrophilicity of aldehydes. Interestingly, it was necessary to adopt two equivalents of allyl β–ketoesters **17a** to aldehydes **17b** in order to achieve high yield of aldol products. Based on their results, Schaus suggested that the second equivalent

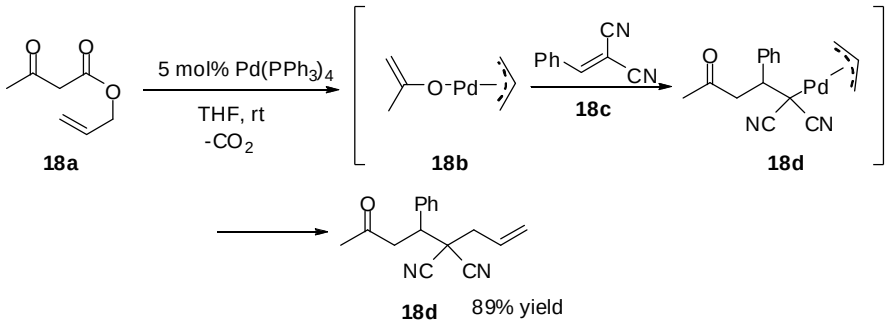
allyl *β*–ketoester reacted with intermediate **17d** to give aldol product **17c** and a metal enolate **17e**, which undergoes allylation to regenerate the Pd(0) catalyst. This hypothesis was supported by separation of a stoichiometric amount allylic alkylation product **17g**.

Scheme 17 *Heterobimetallic-catalyzed decarboxylative aldol reaction*



In addition, electron-poor olefins were also compatible with the above reaction protocol. It has been shown that electron poor olefins such as benzylidene malononitrile **18c**, react with allyl *β*–ketoester **18a** in the presence of $Pd(PPh_3)_4$ to generate **18d** in high yield (Scheme 18).[26] Michael addition of an oxygen-bonded palladium enolate **18d** to activated olefin **18c** produce an intermediate **18d**, which, upon allylation finishes this cascade reaction.[27, 28] However, the substrate scope was not well addressed in this paper, and allyl *β*–ketoester **18a** with an unsubstituted alkene unit was the only one used in their reactions.

Scheme 18 *Pd-catalyzed intermolecular Michael addition with activated olefins*



In conclusion, transition metal-catalyzed allylic alkylation has proven to be an important and convenient tool for organic synthesis, which is still a "hot" topic, and finds many applications in natural products synthesis.[29-33] Yet, despite the significant attention directed toward catalytic allylic alkylation, many challenges still exist.

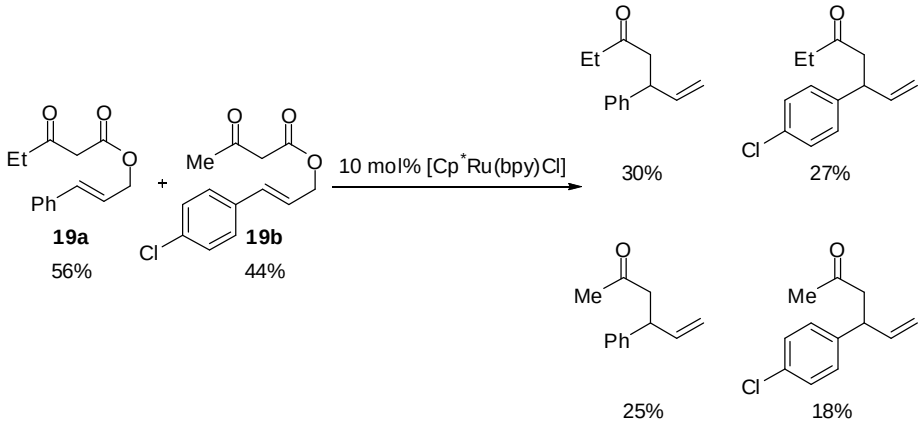
1.3 Ruthenium-Catalyzed Tandem Michael Addition-Allylation

The desire to rapidly generate complex molecules has driven the search for new catalytic processes that effect multiple transformations in one pot. Notable recent examples include tandem cyclization-arylation,[34] allyllation/Pauson-Khand,[35] and olefin metathesis-hydrogenation.[36] All those transformations rely on the ability of a transition metal to catalyze two distinct sequential transformations. On the other hand, a bifunctional catalyst that can simultaneously activate two components of a reaction mixture toward reaction with a third should facilitate multiple concurrent bond-forming reaction with high atomic economy.[37]

During our investigation on transition metal-catalyzed decarboxylative allylation

of allyl β–ketoesters, namely the Carroll rearrangement, we and other have shown that transition metals play two functions, catalyzing the decarboxylative formation of enolate nucleophiles and activating the electrophilic allyl fragment toward nucleophilic substitution.[16, 38, 39] In this regard, a [Cp*Ru(bpy)Cl] complex was shown to catalyze the decarboxylative allylation regioselectively, favoring the branched product (Scheme 9).[16] A crossover experiment was carried out to elucidate the reaction mechanism. Allyl β-ketoesters **19a** and **19b** were prepared and upon treatment with 10 mol% [Cp*Ru(bpy)Cl], all four possible products were formed in a statistical yield (Scheme 19). This result seems to suggest that allyl β-ketoesters are sources of freely diffusing enolates and allylic cations.

Scheme 19 *Cross-over experiment*



Consequently, we were curious whether those enolate intermediates could be trapped by appropriate reactant. As mentioned above, the enolates generated by

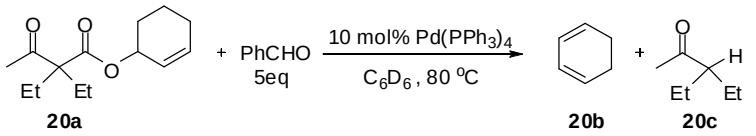
Pd-catalyzed decarboxylation have been intramolecularly intercepted by aldehydes and Michael acceptors.[22, 23] However, the intermolecular version seems to be problematic due to the competing allylation. Recent focus has been directed toward this end. To recap, Schaus reported an intermolecular aldol reaction using a hetero-bimetallic catalyst system (Scheme 17)[25] and Yamamoto found that electron-poor olefins such as benzylidene malononitrile can intercept palladium enolates and undergo intermolecular Michael addition reactions.[26]

1.3.1 Transition-metal Directed Aldol Reaction

Based on those precedents with Pd-enolates chemistry, we decided to investigate the tandem Michael addition-allylation of pronucleophiles under the conditions for Ru-catalyzed decarboxylative allylation.[16] First, different aldehydes were studied since the aldol adducts are synthetically useful. It has been found that *α,α*-disubstitution of the β-ketoester starting materials slows the Carroll rearrangement and consequently, the rearrangement requires higher temperature.[40] The hypothesis here is that, if the competing allylic alkylation is slow, then the generated Pd-enolates could be possibly trapped by aldehydes. To test this hypothesis, disubstituted *β*-ketoester **20a** was prepared and treated with a catalytic amount of $Pd(PPh_3)_4$ in the presence of five equivalents of benzaldehyde (Scheme 20). However, neither the decarboxylative allylation product nor the aldol adducts formed.

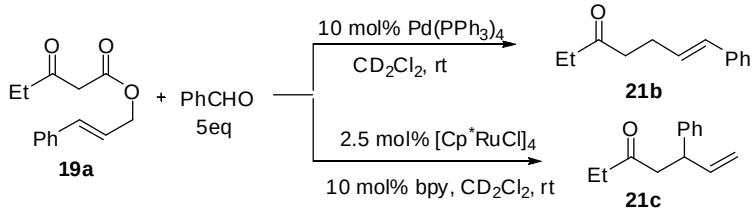
Instead, the competing elimination product **20b** and protonated enolate **20c** were formed exclusively.

Scheme 20 *Pd-enolate directed aldol reaction*



Following that, starting material **19a** was synthesized and allowed to react with benzaldehyde in the presence of palladium catalyst. Unfortunately, the linear decarboxylative allylic alkylation product **21b** was produced. Similarly, when a ruthenium complex was employed as the catalyst, the branched allylation product **21c** was formed and no aldol reaction products were observed (Scheme 21).

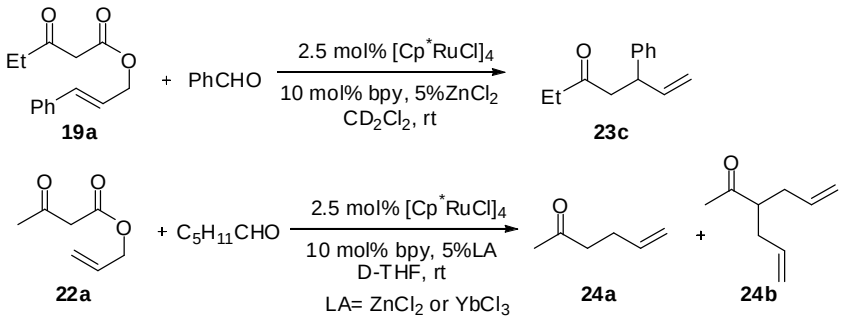
Scheme 21 *Pd-enolate directed aldol reaction*



In the light of Schaus' strategy,[25] Lewis acids were also incorporated as a cocatalyst in an attempt to activate aldehydes toward nucleophilic addition. However both $ZnCl_2$ and $YbCl_3$, which were shown to be the most effective Lewis acids by Schaus, failed in our case and only decarboxylative allylation products, such as **21c**,

24a-b were produced as shown in Scheme 22. The possible reason could be either that the Lewis acids were not compatible with the ruthenium catalyst complex or that the Lewis acids did not activate the aldehyde enough to be trapped by the enolate intermediates. Besides, other solvents, such as THF, CH_3CN and CH_2Cl_2 were used, and it was found that solvent effects were negligible. In most case, decarboxylative allylation products were formed as the major products, even though in some cases, trace amounts of aldol adducts were generated. As to substrate **22a**, a combination of palladium with different phosphine ligands and Lewis acids were also studied. Surprisingly, no reaction occurred and the starting material stayed intact over the course of the reaction.

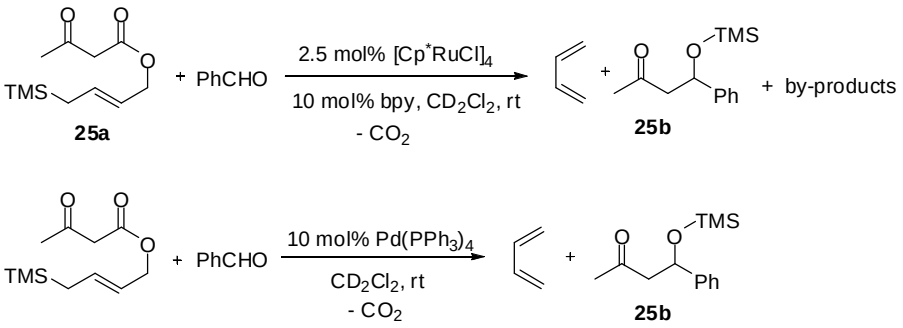
Scheme 22 *Attempted use of Lewis acids to facilitate a directed aldol reaction*



Even though standard allyl β-ketoesters did not undergo intermolecular aldol reactions, silyl β-ketoester **25a** showed interesting reactivity toward benzaldehyde (Scheme23). With the ruthenium complex, only 65% of the starting material **25a** underwent decarboxylation after 48 hours and small amount of the aldol product **25b**

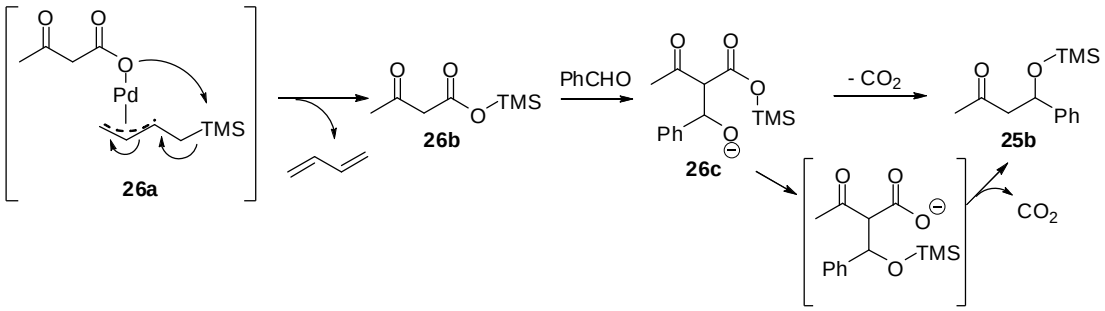
was formed along with by-products; whereas $Pd(PPh_3)_4$ has shown super catalytic activity, the decarboxylation completed in 10 minutes and the aldol adduct **25b** was generated cleanly in one hour (95% NMR yield).

Scheme 23 *Pd-enolate directed aldol reaction with silyl β-ketoester*



The successful aldol reaction can be rationalized as follows. The expected oxidative addition reaction would produce π-allylpalladium complex **26a** which undergoes a desilylation reaction to generate 1,3-butadiene and intermediate **26b**, which was supported by the formation of a new proton signal at 3.5 ppm in the ^1H NMR spectrum of the reaction mixture. Aldol reaction generates intermediate **26c**, which then undergoes intramolecular silyl transfter, followed by decarboxylation to furnish product **25b** as shown in Scheme 24.

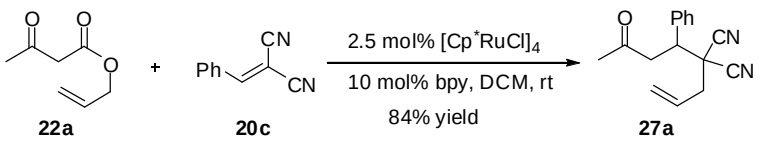
Scheme 24 *Possible pathways*



1.3.2 Transition Metal-Catalyzed Michael Addition-Allylation Reactions

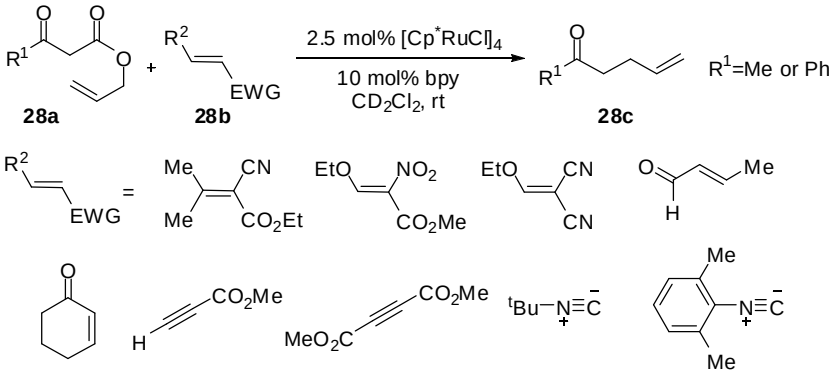
It has been shown that Michael additions to electron-poor olefins ($RCH=CZ_2$) generate stabilized nucleophiles, which are well known to undergo transition metal facilitated allylic alkylation. Thus, we expected that ruthenium would be a competent catalyst for a tandem Michael addition-allylation reaction. Fortunately, benzylidene malononitrile smoothly reacted with the unsubstituted allyl *β*–ketoesters **22a** under the condition of previously developed for catalytic Carroll-type rearrangement, affording the desired product **27a** in high yield as shown in Scheme 25.[41] Thus, activated Michael acceptors are ideally set up to undergo tandem enolate addition and allylation. Furthermore, it was envisioned the regiochemistry of allylation could be controlled by the appropriate choice of the transition metal catalyst.[12, 42]

Scheme 25 *Reaction conditions for decarboxylative olefin insertion*



To begin, a range of Michael acceptors were investigated to test their compatibility with the above reaction conditions. Based on the screening results, it was found that the electrophilicity of the Michael acceptors/electrophile is crucial for the successful decarboxylative olefin insertion. The unsuccessful Michael acceptors **28b** are shown in Scheme 26. Except for DMAD, a strong π-acid known to deactivating the transition metal catalysts through coordination, all other Michael acceptors did not undergo the tandem Michael addition-allylation reactions and the Carroll rearrangement products **28c** were formed exclusively.

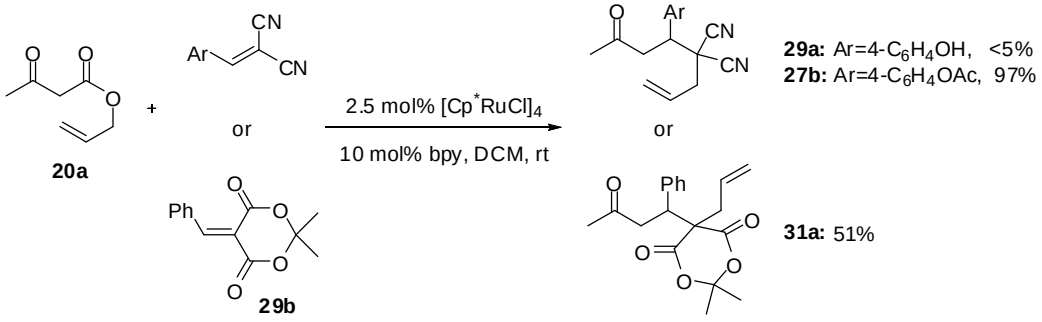
Scheme 26 *Unsuccessful Michael acceptors*



After that, our attention was focused on the benzylidene malononitrile derivatives, which have been shown to efficiently trap the Pd-enolates as illustrated previously in Scheme 27. Various β-ketoesters and malononitriles were prepared. Interestingly, the electronics of the malononitrile are crucial to the success of the decarboxylative insertion. When *p*-hydroxybenzylidene malononitrile (electrophilicity, E= -10.8)[43]

was employed as the electrophile, Michael addition-allylation product **29a** was obtained in <5% yield, in which the decarboxylation-allylation product was formed exclusively (Scheme 27). This issue was addressed by simply acylation of the hydroxyl group and in that case, Michael addition-allylation product **27b** was obtained in 97% isolated yield.[43]

Scheme 27 *Effects of the electrophilicity of Michael acceptors*

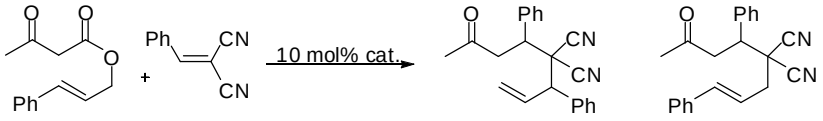


The most successful reactions achieved were those with olefins containing two electron-withdrawing groups, which is consistent with their electrophilicity parameters (**18c**, Ar=Ph, E= -9.42).[43] Also shown in Scheme 27 is a Meldrum's acid derivative **29b** that is an effective Michael acceptor, showing that activated diesters are also viable reaction partners. Yamamoto has shown that Michael acceptors with acyclic diesters do not undergo tandem Michael addition-allylation reactions under palladium catalysis, which was attributed to lack of coplanarity of the two esters due to the sterics.[26] Whereas in the case of Meldrum's acid derivative **29b**, the six-membered ring helps to lock the coplanarity of the ester groups, enhancing the

electrophilicity of the olefin.

Next, we turned our attention to developing the first regioselective tandem Michael addition-allylic alkylation of activated Michael acceptors. It was gratifying to find that treatment of **30a** with benzylidene malononitrile, 2.5 mol % $[Cp^*RuCl]_4$, and 10 mol % bipyridine at room temperature in methylene chloride produced **27c** in high yield (89%) and over 19:1 regioselectivity (dr = 1.9:1) (Scheme 28). The analogous palladium-catalyzed reaction produced the opposite regioisomer **30b** in 80% yield. The regioselectivities for ruthenium and palladium catalysts are consistent with those observed for other allylation reactions.[5, 12, 26]

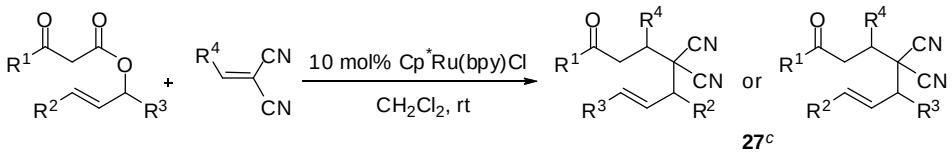
Scheme 28 *Catalyst-dependent regioselectivity*



A variety of allyl *β*-ketoesters undergo smooth decarboxylative coupling with Michael acceptors (Table 1). Variation of the R^1 group shows that the reaction is typified by regiospecific formation of enolates (Scheme 28). Of note here is that the diastereoselectivity of products **27c** and **27i**, formed from the unsubstituted allyl partners are generally higher than those synthesized from the other regioisomers. This observation is interesting and deserves further attention. It is noteworthy that

equilibration of the kinetic enolate does not occur even when R^1 is benzyl and there is a large thermodynamic driving force favoring the formation of the stabilized enolate. In fact, previous attempts to generate the terminal enolate of phenylacetone by deprotonation have failed.[44, 45]

Table 1 *Yields of tandem ruthenium-catalyzed Michael addition-allylations*



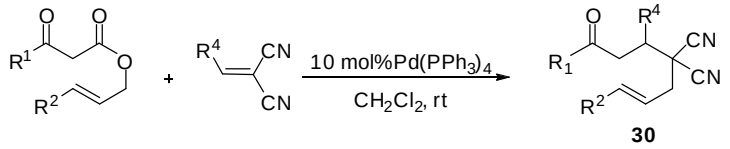
27[c]

R^1	R^2	R^3	R^4	Prod.	Time (h)[a]	% Yield (dr)[b]
Me	H	H	Ph	**27a**	2	84
Me	H	H	*p*-C_6H_4OAc	**27b**	5	97
Me	Ph	H	Ph	**27c**	12	89 (1.9:1)
Me	H	Ph	Ph	**27c**	6	85 (3.5:1)
Bn	H	H	Ph	**27d**	4.5	87
Ph	H	H	Ph	**27e**	5.5	64
Et	Ph	H	Ph	**27f**	22	93 (1.8:1)
Me	H	*p*-C_6H_4OMe	Ph	**27g**	18	62 (1.6:1)
Me	H	*p*-C_6H_4OCl	Ph	**27h**	19	62 (1.8:1)
Me	Ph	H	*p*-C_6H_4OAc	**27i**	48	92 (2.7:1)
Me	H	Ph	*p*-C_6H_4OAc	**27i**	16	76 (4.5:1)

[a] Unless otherwise mentioned, the reaction was carried out with allyl β-ketoester (0.2 M), Michael acceptor (0.2 M), $[Cp^*RuCl]_4$ (0.005 M), and bpy (0.02 M) in CH_2Cl_2 at room temperature. [b] Isolated yield after column chromatography. [c] The branched product was formed exclusively, with references to the size of substituent s R_2 and R_3.

For the reason of comparison, two allyl β-ketoesters were treated with 10 mol% $Pd(PPh_3)_4$ in the presence of one equivalent Michael acceptors, affording the opposite regioisomers **30b**, **30c** in high yield (Table 2).

Table 2 *Yields of Pd-catalyzed tandem Michael addition-allylation*



30

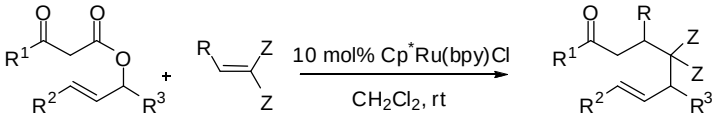
R^1	R^2	R^4	Prod.	Time (h)[a]	% Yield[b]
Me	Ph	Ph	**30b**	13	80
Et	Ph	Ph	**30c**	17	88

[a] Unless otherwise mentioned, the reaction was carried out with allyl β-ketoester (0.2 M), Michael acceptor (0.2 M) and $Pd(PPh_3)_4$ (0.02 M) in CH_2Cl_2 at room temperature. [b] Isolated yield after column chromatography.

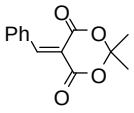
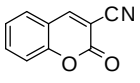
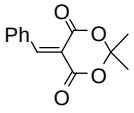
One application of the tandem Michael addition-allylation reaction protocol was found in the modification of coumarin derivatives, and product **31b** was obtained in 45% yield; however the product was formed cleanly based on ^{1}H NMR spectrum. This could serve as a rapid way for modifying coumarin, which is the core structure of many biologically active compounds.[46, 47] Also shown in Table 3 is a Meldrum's acid derivative, which functions as efficient Michael acceptors to furnish products **31a** and **31c** in good yields. Of note here is that the formation of product **31c** was catalyzed by $Pd(PPh_3)_4$; whereas when [Cp*Ru(bpy)Cl] was employed as the catalyst,

the Carroll rearrangement product was produced as the major one. This is possibly due to the steric hindrance of cyclopentene ring but it illustrates the trend that palladium catalysts are generally more active toward tandem Michael addition-allylation than the corresponding ruthenium catalysts. This hypothesis was further supported by the longer reaction times when [Cp*Ru(bpy)Cl] catalyst was adopted as the catalyst, comparing with that of Pd catalyst. For example, product **31c** was formed in 12 hours with $Pd(PPh_3)_4$; while with [Cp*Ru(bpy)Cl] catalyst, the reaction did not go to completion even after 180 hours. It is noteworthy that the diastereoselectivity of addition to the cyclic Michael acceptor is much higher than that observed for benzylidene malononitrile derivatives, in which a less constrained transition state is involved (Table 1).

Table 3 *Yields of tandem Michael addition-allylation of other Michael acceptors*



31

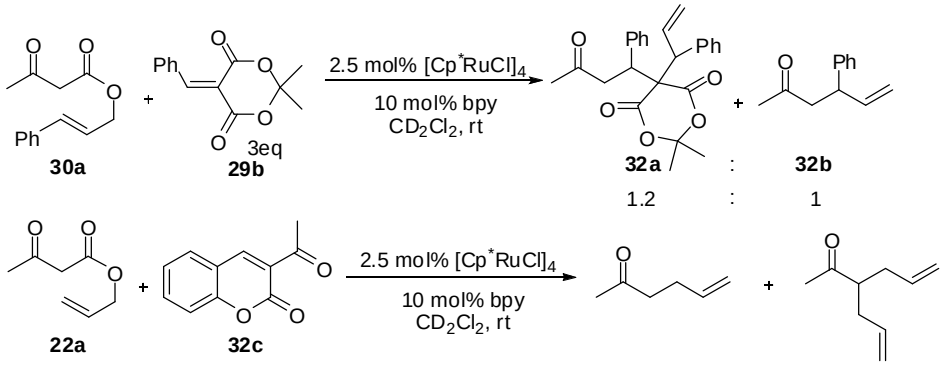
R^1	R^2	R^3	Michael acceptor	Prod.	Time (h)[a]	% Yield (dr)[b]
Me	H	H		**31a**	1.5	51
Me	H	H		**31b**	2	45 (12:1)
Me			 	**31c**[c]	1.5	65 (5.5:1)

[a] Unless otherwise mentioned, the reaction was carried out with allyl β-ketoester (0.2 M),

Michael acceptor (0.2 M) and $[Cp^*RuCl]_4$ (0.005 M), and bpy (0.02 M) in CH_2Cl_2 at room temperature. [b] Isolated yield after column chromatography. [c] using 10 mol% $Pd(PPh_3)_4$.

Following that, more diesters and β-ketoester derivatives were investigated and the results are summarized in Scheme 29. In the presence of a [Cp*Ru(bpy)Cl] catalyst, allyl β–ketoesters **30a** reacted with three equivalents of Meldrum's acid derivative **29b**, affording a mixture of Michael addition-allylation product **32a** and Carroll rearrangement product **32b** in a ratio of 1.2:1. We propose that the bulky styrene unit accounts for the lower selectivity, similar to cyclopentene derivative mentioned above. Since cyanocoumarin has shown to be effective Michael acceptors, 3-acetyl coumarin **32c** was also examined as a partner for decarboxylative olefin insertion; however the Carroll rearrangement products were formed instead.

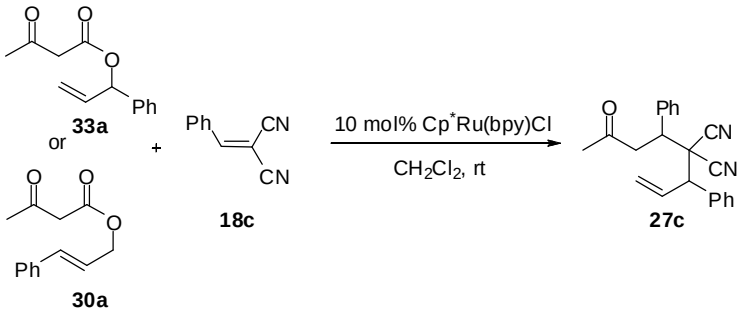
Scheme 29 *Tandem Michael addition-allylation with lower chemoselectivity*



While we expected that the above reactions involved π-allyl ruthenium intermediates, this was confirmed by the reactions of regioisomeric allyl β-ketoesters **33a** and **30a** which give the same product **27c** (Scheme 30). Thus the reaction

regiospecifically generates enolates followed by regioselective allylation. Interestingly, the less substituted olefin reactant **33a** provides product more rapidly. Consistent with this trend, the unsubstituted allyl partners generally react most quickly. This implies that coordination of the alkene to ruthenium may be important prior to, or in, the rate-limiting step.

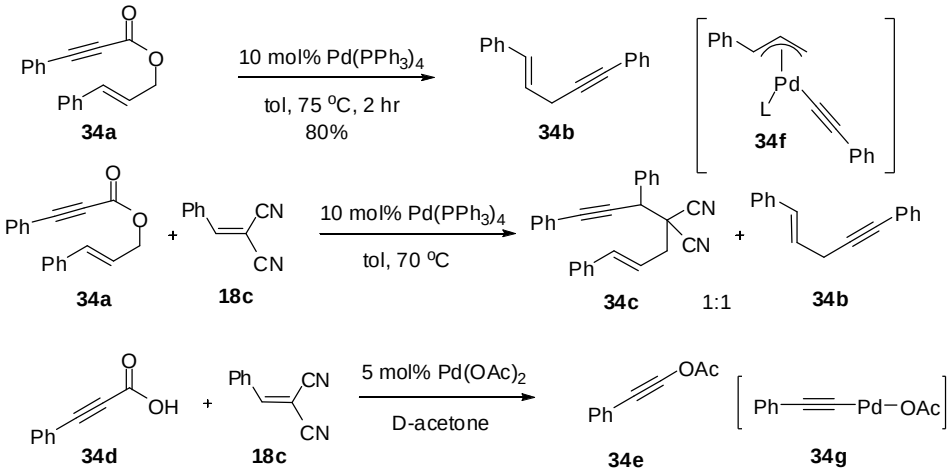
Scheme 30 *Regioselective allylation*



Our group has a long-standing interest in decarboxylative allylation reactions. In 2005, Dinesh reported a decarboxylative allyl-acetylide coupling of **34a** to form 1,4-enyne product **34b**, in which a palladium-allyl-acetylide intermediate **34f** was thought to be involved as shown in Scheme 31.[48] Consequently, we were curious whether the Pd-acetylide intermediate can be trapped by Michael acceptors. However, treatment of the propiolate ester **34a** with benzylidene malononitrile **18c** yielded a mixture of products **34c** and **34b** in almost 1:1 ratio. Phenyl propiolic acid **34d** was also studied in this context, in which palladium acetate was employed as the catalyst to facilitate the generation of a Pd-acetylide intermediate **34g**. Surprisingly, reductive

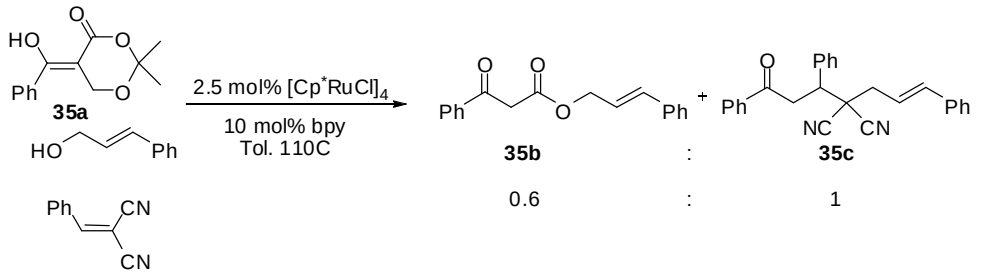
elimination occurred predominantly over insertion reaction, and Pd black was formed along with acetic acid which in turn supported the formation of proposed intermediate **34g**. The product structure was tentatively assigned as **34e**.

Scheme 31 *Tandem Michael addition-allylation with Pd-acetylide intermediate*



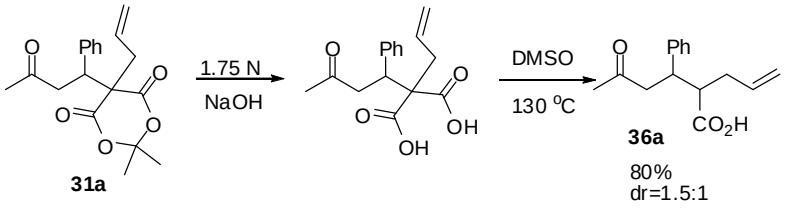
To further expand our tandem Michael addition-allylation, a three-component coupling reaction was investigated (Scheme 32). Here toluene was chosen as the solvent because of the need for *in situ* formation of allyl *β*–ketoester **35b**. Interesting, the linear product **35c** was produced with a pair of diastereotopic protons signal at 2.6 and 2.7 ppm, along with unreacted starting material **35b** in a ratio of 0.6:1. The reaction was also carried out with $Pd(PPh_3)_4$ as the catalyst, in which a messy mixture was generated with recovery of cinnamyl alcohol.

Scheme 32 *Three components coupling reactions*



Finally, to illustrate the utility of the benzylidene diester electrophiles, we performed a simple hydrolysis and decarboxylation of **31a** (Scheme 33). Products like the resulting γ,δ-unsaturated acid **36a**, are particularly useful substrates for halolactonizations.[49]

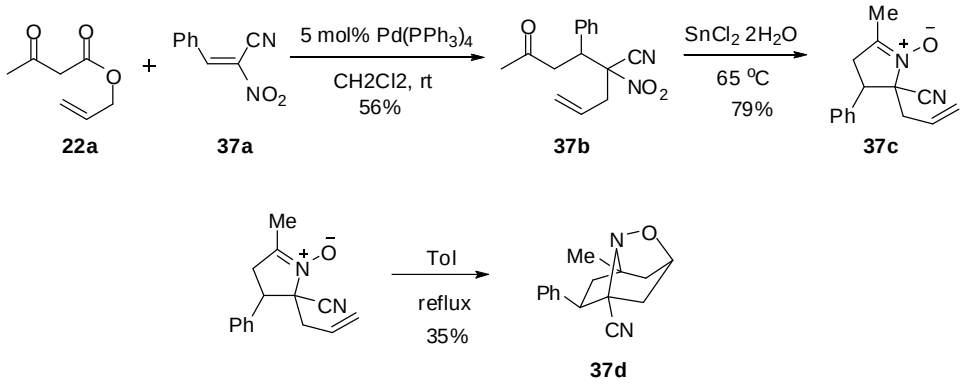
Scheme 33 *Utility of the benzylidene Meldrum's derivatives*



Another noteworthy application could be found in the rapid synthesis of polycyclic tropane alkaloid precursor **37d**. Michael acceptor **37a** bearing a nitro group was prepared and reacted with allyl-β-ketoester **22a** to form the insertion product **37b**, which was partially reduced to hydroxyl amine followed by cyclization to generate nitrone product **37c**. Upon refluxing in toluene, intramolecular [3+2] cycloaddition afforded the polycyclic ring system.[50, 51] The efficient ring construction

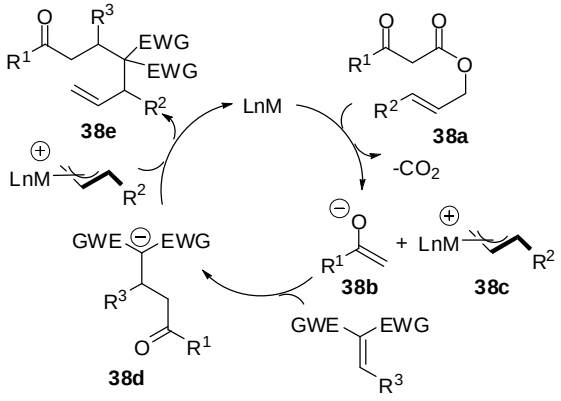
strategy was not followed up due to time constraints.

Scheme 34 *Tropane alkaloid ring synthesis*



The tandem Michael addition-allylic alkylations involved in all of the above reactions are thought to start by oxidative addition the allylic ester, followed by decarboxylation to generate freely diffusing enolates **38b** and π-allyl species **38c** (Scheme 35). The addition enolates to activated Michael acceptors ($RCH{=}C(EWG)_2$) produces stabilized enolates **38d**, which are well-known nucleophiles for metal-catalyzed allylic substitution to produce product **38e** and regenerate the catalyst.[5]

Scheme 35 *Catalytic cycle of Tandem Michael addition-allylation*



In conclusion, we have developed a regioselective, catalytic coupling of enolates, Michael acceptors, and allyl electrophiles. The tandem Michael addition-allylation is made possible by the decarboxylative activation of allyl β-ketoesters to produce enolates and π-allyl metal electrophiles. We are currently exploring similar reactions that exploit our ability to regiospecifically generate enolates from β-keto esters at room temperature under base-free conditions.

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Appendix A

Experimental Procedures and Data for Chapter 1

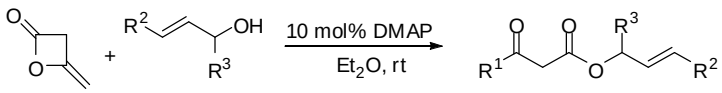
General Experimental

THF was dried over sodium metal. Toluene, methylene chloride and diethyl ether were dried over activated alumina on a solvent system purchased from Innovative Technology, Inc.[1] Acetonitrile and 1,4-dioxane were dried and stored over activated molecular sieves. Commercially available reagents were used without additional purification unless otherwise stated. Products were purified on silica gel from Sorbent Technologies (230x400 mesh, 60 Å porosity, pH 6.5-7.5). Ruthenium and palladium compounds were obtained from Strem. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5715-7, EMD chemicals). UV lamp (254 nm) or $KMnO_4$ stain were used for monitoring TLC plates.

^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance 400 or Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals. Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, and HMQC spectroscopies and X-ray data. High resolution mass spectrometry was performed on an AUTOSPEC-Q tandem hybrid mass spectrometer (VG Analytical Ltd, Manchester, UK). High resolution mass spectrometry was performed on a LCT Premier (Waters Corp., Milford MA) time of flight mass spectrometer. FTIR spectra were acquired on a Shimadzu FTIR-8400S spectrometer. HPLC analysis was performed on a Shimadzu SCL-10A VP instrument.

Preparation of Starting Materials

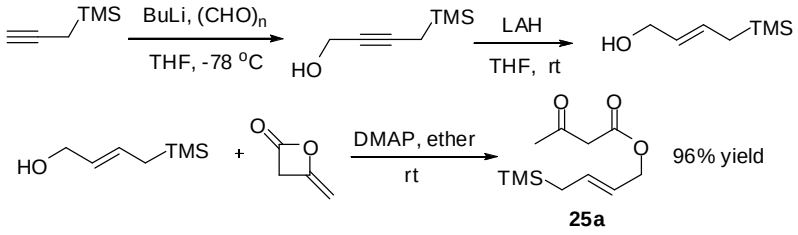
Generally, allyl β-ketoesters were synthesized by the DMAP catalyzed coupling reaction between commercially available allylic alcohols with diketene, followed by purification via flash column chromatography when R^1 equals to methyl group. (SiO_2, 7:1 hexane: ethyl acetate).[2]



For silyl allyl β-ketoester **25a**, the allylic alcohol was prepared,[3] followed by coupling with diketene.[2] To a solution of propargyl triethylsilane (500 mg, 4.4 mmol) in 5 mL THF at -78 ^oC under argon was added n-butyl lithium (4.9 mmol, 1.1 eq.) dropwise, and the reaction mixture was stirred at -78 ^oC for 0.5 hour before adding paraformaldehyde (4.9 mmol, 1.1 eq.) portion wise. The mixture was warmed to room temperature and kept stirring overnight. The reaction was quenched with sat. NH_4Cl solution, extracted with EtOAc. The organic phase was washed with brine, dried over $MgSO_4$ and concentrated to give the crude product, which was taken to the next step without further purification.

To a solution of LAH (340 mg, 8.8 mmol, 2.0 eq.) in 15 mL THF under argon was slowly added a solution of crude alkyne (4.4 mmol) in 5 mL THF via cannulation. The reaction mixture was then heated to reflux for 1hr, followed by quenching with water which was monitored by the release of hydrogen. The resulting mixture was filtered over a celite pad, dried over $MgSO_4$ and the solvent was removed to afford the corresponding allylic alcohol.

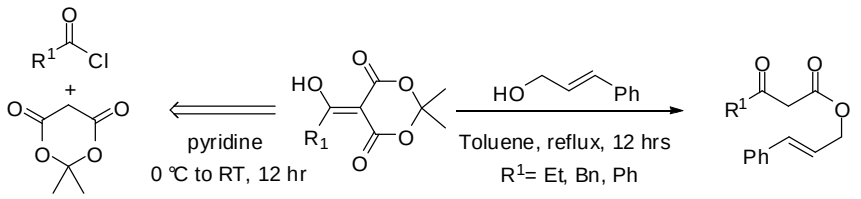
To a solution of the allylic alcohol (225 mg, 1.6 mmol) in 10 mL ether under argon was added diketene in one protion (1.8 mmol, 1.1 eq.), followed by DMAP (17.6 mg, 0.16 mmol, 0.1 eq). The reation mixture was kept stirring until reaction completion indicated by TLC (generally 1.5 hr). The reaction was quenched with sat. NH_4Cl solution, extracted with ether. The organic phase was washed with brine, dried over $MgSO_4$ and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 10:1 hexane: ethyl acetate).



25a

If R^1 is a group other than methyl, then the allyl β-ketoesters were synthesized by the condensation of the corresponding acid chloride with Meldrum's acid,[4] followed by addition of the appropriate allylic alcohol.[5]

To a solution of the Meldrum's acid (1.5 g, 10.4 mmol) in 20 mL dichloromethane at 0 °C under argon was added pyridine (26.0 mmol, 2.5 eq.) over 5 mins, followed by propionyl chloride (10.4 mmol, 1.0 eq.) over 20 mins. The resulting orange mixture was kept stirring until reaction completion indicated by TLC (generally 12 hrs). The reaction mixture was poured to a mixture of ice and HCl (2 M/L), extracted with dichloromethane, dried over $MgSO_4$ and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 8:1 hexane: ethyl acetate).



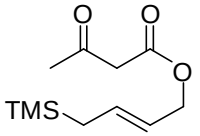
General procedure for ruthenium-catalyzed tandem Michael-allylation:

In a Schlenk tube under argon, $[Cp^*RuCl]_4$ (2.5 mol %), bipyridine (10 mol %), allyl β-ketoester (1 mmol) and malonitrile (1 equiv.) were dissolved in 5 mL of methylene chloride. The resulting deep purple solution was stirred at room temperature under Ar. The reaction was monitored by TLC. Following solvent evaporation the crude product was purified via flash chromatography (SiO_2, 6:1 hexane: ethyl acetate), providing the products in > 95% purity as determined by ^1H NMR spectroscopy.

General procedure for the palladium-catalyzed tandem Michael-allylation:

In a Schlenk tube under argon, $Pd(PPh_3)_4$ (10 mol %), allyl β-ketoester (1 mmol) and malonitrile (1 equiv.) were dissolved in 5 mL of methylene chloride. The resulting yellow solution was stirred at room temperature under Ar. The reaction was monitored by TLC. Following solvent evaporation the crude product was purified via flash chromatography (SiO_2, 6:1 hexane: ethyl acetate), providing the products in > 95% purity as determined by ^1H NMR spectroscopy

Spectroscopic Data



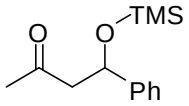
(*E*)-4-(trimethylsilyl)but-2-enyl 3-oxobutanoate

27a (cw1067)

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.08 (0.1 H, br. S.: C**H**(OH)=), 5.85 (1H, ddd, *J*=15.2, 8.3, 8.2 Hz: TMSCH_2C**H**=), 5.45 (1H, m: C**H**=), 4.57 (2H, d, *J*=6.8 Hz: **C**H_2CO), 3.46 (s, 2H: C(O)C**H**$_2$), 2.26 (3H, s: C(O)C**H**$_3$), 1.56 (2H, dd, *J*=8.2, 0.5 Hz: C**H**$_2$TMS), 0.04 (s, 9H: C**H**$_3$(TMS)).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 203.95 (**C**=O), 167.5 (**C**O_2), 135.20 (**C**H=), 122.05 (TMSCH_2**C**H=), 66.97 (O**C**H_2), 50.68 (**C**H_2CO), 30.52 (**C**H_3CO), 23.49 (TMS**C**H_2), -1.86 (**C**H_3(TMS)).

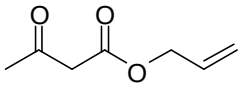


4-phenyl-4-(trimethylsilyloxy)butan-2-one

25b (cw1070)

$Pd(PPh_3)_4$: 95% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (m, 4H: arom H), 7.28 (m, 1H: arom H), 5.18 (dd, 1H, *J*=8.8, 4.0 Hz: C**H**Ph), 2.93 (dd, 1H, *J*=15.2, 8.8 Hz: C(O)C**H**$_2$), 2.61 (dd, 1H, *J* =15.3, 4.0 Hz: C(O)C**H**$_2$), 2.15 (s, 3H: C(O)C**H**$_3$), 0.03 (s, 9H: C**H**$_3$(TMS)).



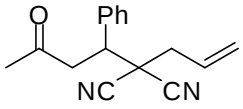
allyl 3-oxobutanoate

22a (cw1083)

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.05 (0.1 H, br. S.: C**H**(OH)=), 5.95 (1H, m: C**H**=), 5.37 (1H, d, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 5.28 (1H, d, *J*=11.7 Hz: CH=C**H**(*H*)$_Z$), 4.65 (2H, d, *J*=6.8 Hz: **C**H_2O), 3.51 (s, 2H: C(O)C**H**$_2$), 2.27 (3H, s: C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 201.0 (**C**=O), 167.3 (**C**O_2), 132.4 (**C**H=), 118.8 (=**C**H_2), 66.3 (O**C**H_2), 50.5 (**C**H_2CO), 30.6 (**C**H_3CO).



2-allyl-2-(3-oxo-1-phenylbutyl)malononitrile

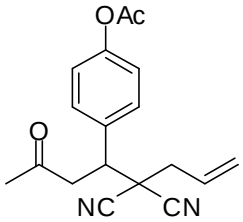
27a[6] (cw1110)

colorless oil

[Cp*Ru(bpy)Cl]: 84% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, 5H: arom H), 5.98-5.88 (m, 1H, *J* = 10.1, 6.8, 7.3, 7.1 Hz: =C**H**), 5.43 (d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_Z$), 5.23 (d, 1H, *J* = 6.8 Hz: CH=C**H**(*H*)$_E$), 3.78 (dd, 1H, *J* =10.4, 3.5 Hz: C(O)CH$_2$C**H**Ph), 3.44 (dd, *J* =10.4, 17.4 Hz, 1H: C(O)C**H**$_2$), 3.22 (dd, *J* =3.5, 17.4 Hz, 1H: C(O)C**H**$_2$), 2.56(dd, *J* =7.3, 14.1 Hz, 1H: C**H**$_2$CH=), 2.42(dd, *J* =7.1, 14.1 Hz, 1H: C**H**$_2$CH=), 2.13(s, 3H: C(O)C**H**$_3$);

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.95 (**C**=O), 136.15 (Quat.), 129.54 (=**C**H), 129.54 (Arom. **C**H), 123.36 (=**C**H$_2$), 115.66 (**C**N), 114.91 (**C**N), 46.25 (**C**HPh), 46.10 (C(O)**C**H$_2$), 43.52 (**C**(CN)$_2$), 40.73 (**C**H$_2$CH=), 30.86 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, and HMQC spectroscopies.



2-[1-[4-(acetyloxy)phenyl]-3-oxobutyl]-2-(2-propen-1-yl)-propanedinitrile

27b (cw1126)

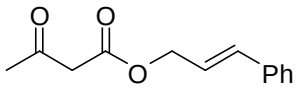
colorless oil

[Cp*Ru(bpy)Cl]: 97% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (m, *J* = 8.6, 2H: arom H), 7.14 (m, *J* = 8.6, 2H: arom H) 5.93-5.83 (m, 1H, *J* = 10.1, 17.4, 7.6, 5.8 Hz: =C**H**), 5.43 (d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_E$), 5.34 (d, 1H, *J* = 17.4 Hz: CH=C**H**(*H*)$_Z$), 3.80 (dd, 1H, *J* =3.5, 9.8 Hz: C(O)CH$_2$C**H**), 3.36 (dd, *J* =9.8, 17.7 Hz, 1H: C(O)C**H**$_2$), 3.20 (dd, *J* =3.5, 17.7 Hz, 1H: C(O)C**H**$_2$), 2.47(dd, *J* =7.6, 13.9 Hz, 1H: C**H**$_2$CH=), 2.39(dd, *J* =5.8, 13.9 Hz, 1H: C**H**$_2$CH=), 2.32(s, 3H: OC(O)C**H**$_3$), 2.15(s, 3H: C(O)C**H**$_3$).

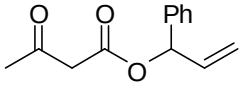
^{13}C NMR (100 MHz, $CDCl_3$) δ 203.40 (**C**=O), 169.27 (O**C**=O), 151.24 (Quat.), 132.95 (Quat.), 130.05 (Arom. **C**H), 128.56 (=**C**H), 123.66 (=**C**H$_2$), 122.53 (Arom. **C**H), 115.17 (**C**N), 114.44 (**C**N), 46.32 (C(O)**C**H$_2$), 45.30 (**C**HAr), 42.98 (**C**(CN)$_2$), 40.37 (**C**H$_2$CH=), 30.75 (**C**H$_3$), 21.35 (OC(O)**C**H$_3$).

FTIR ($CDCl_3$): ν_{max} 3062, 2252, 1770, 1724, 1425, 989, 914.
HRMS calcd for $C_{18}H_{18}N_2O_3Na$ [M+Na] 333.1215, found 333.1208.



cinnamyl 3-oxobutanoate
20a[7] (cw1098)
colorless oil

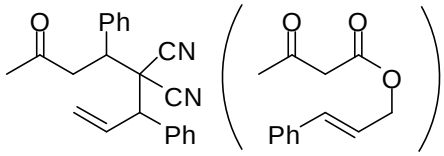
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.07 (0.1 H, s: C**H**(OH)=), 7.42 (2H, m: arom H), 7.35 (2H, t, *J*=7.3 Hz: arom H), 7.30 (1H, d, *J*=7.0 Hz: arom H), 6.70 (1H, d, *J*=15.9 Hz: PhC**H**=), 6.30 (1H, dt, *J*=15.8, 6.7 Hz: C**H**), 4.83 (2H, d, *J*=6.5 Hz: C**H**$_2$O), 3.53 (s, 2H: C(O)C**H**$_2$), 2.31 (3H, s: C(O)C**H**$_3$).



1-phenylallyl 3-oxobutanoate
33a (cw1133)
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (5H, m: arom H), 6.33 (1H, dt, *J*=6.0, 1.2 Hz: PhC**H**), 6.04 (1H, ddd, *J*=17.0, 10.6, 5.9 Hz: C**H**=), 5.33 (2H, m: =C**H**$_2$), 3.53 (2H, s: C(O)C**H**$_2$), 2.26 (3H, s: C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 200.8 (**C**=O), 138.6 (Quat. arom. **C**), 166.5 (**C**O_2), 136.0 (**C**H=), 129.0 (Arom. **C**H), 128.9 (Arom. **C**H), 128.9 (Arom. **C**H), 127.6 (Arom. **C**H), 118.1 (=**C**H_2), 77.7 (O**C**H), 50.7 (**C**H_2CO), 30.6 (**C**H_3CO).

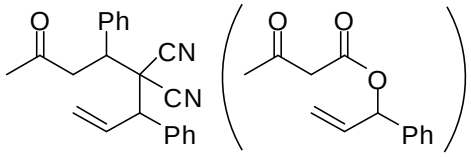


2-(3-oxo-1-phenylbutyl)-2-(1-phenylallyl)malononitrile

27c (cw1104)

colorless oil

[$Cp^*Ru(bpy)Cl$]: 89% yield, dr = 1.9



2-(3-oxo-1-phenylbutyl)-2-(1-phenylallyl)malononitrile

27c (cw1138)

colorless oil

[$Cp^*Ru(bpy)Cl$]: 85% yield, dr = 3.5

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.50-7.28 (m, 10H: arom H), 6.41-6.32 (m, 1H, *J* = 16.9, 10.4, 9.1 Hz: =C**H**), 5.53 (d, 1H, *J* = 10.4 Hz: CH=C**H**$(H)_E$), 5.23 (d, 1H, *J* = 16.9 Hz: CH=C**H**$(H)_Z$), 3.87 (dd, 1H, *J* =10.6, 3.3 Hz: C(O)CH_2C**H**Ph), 3.45-3.38 (m, 2H: overlapping C**H**Ph, C(O)C**H**$_2$), 3.22 (dd, *J* =17.4, 3.3 Hz, 1H: C(O)C**H**$_2$), 2.09 (s, 3H: C(O)C**H**$_3$).

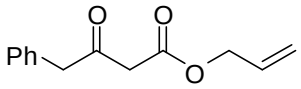
Minor diastereoisomer: δ 7.50-7.28 (m, 10H: arom H, overlapping minor/major isomers), 6.44-6.30 (m, 1H, overlapping minor/major isomer: =C**H**), 5.47 (d, 1H, *J* = 10.1 Hz: CH=C**H**$(H)_E$), 5.36-5.26 (d, 1H, overlapping minor/major isomer: CH=C**H**$(H)_Z$), 3.76 (dd, 1H, *J* =10.6, 3.0 Hz: C(O)CH_2C**H**Ph), 3.45-3.38 (m, 2H: overlapping C**H**Ph, C(O)C**H**$_2$), 3.08 (dd, *J* =17.2, 3.0 Hz, 1H: C(O)C**H**$_2$), 2.06 (s, 3H: C(O)C**H**$_3$);

^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 203.76 (**C**=O), 137.10 (Quat.), 135.52 (Quat.), 132.40 (=**C**H), 129.34 (Arom. **C**H), 129.35 (Arom. **C**H), 128.73 (Arom. **C**H), 122.90 (=**C**H_2), 115.13 (**C**N), 114.21 (**C**N), 52.90 (**C**HPh), 48.65 (**C**$(CN)_2$), 46.85 (C(O)**C**H_2), 44.68 (C(O)CH_2**C**HPh), 30.94 (CH_3).

Minor diastereoisomer: δ 203.76 (overlapping **C**=O), 136.65 (Quat.), 135.20 (Quat.), 133.84 (=**C**H), 129.58-128.91 (overlapping minor/major isomer: Arom. **C**H), 121.88 (=**C**H_2), 115.09 (**C**N), 114.63 (**C**N), 53.09 (overlapping with solvent: **C**HPh), 48.84 (overlapping minor/major isomer: **C**$(CN)_2$), 45.76 (C(O)**C**H_2), 44.71 (overlapping minor/major isomer: C(O)CH_2**C**HPh), 30.85 (overlapping minor/major isomer: CH_3).

FTIR ($CDCl_3$): ν_{max} 3053, 2304, 1724, 1421, 991, 895.

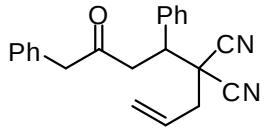
HRMS calcd for $C_{22}H_{20}N_2ONa$ [M+Na] 351.1473, found 351.1468.



allyl 3-oxo-4-phenylbutanoate
cw1150
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.06 (0.1H, s: C**H**(OH)=), 7.36 (2H, q, *J*=7.1 Hz: arom H), 7.32 (1H, d, *J*=7.5 Hz: arom H), 7.23 (2H, d, *J*=7.5 Hz: arom H), 5.92 (1H, m: C**H**=), 5.35 (1H, d, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 5.28 (1H, d, *J*=10.4 Hz: CH=C**H**(*H*)$_Z$), 4.63 (2H, d, *J*=7.0 Hz: C**H**$_2$O), 3.86 (2H, s: PhC**H**$_2$), 3.51 (2H, s: C(O)C**H**$_2$),.

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 200.7 (**C**=O), 167.2 (**C**O_2), 133.5 (Quat. arom. **C**), 131.9 (**C**H=), 130.0 (Arom. **C**H), 129.3 (Arom. **C**H), 127.8 (Arom. **C**H), 119.4 (=**C**H_2), 66.5 (O**C**H_2), 50.5 (Ph**C**H_2), 48.6 (**C**H_2CO).



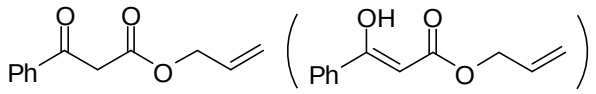
2-allyl-2-(3-oxo-1,4-diphenylbutyl)malononitrile
27d (cw1153)
colorless oil
[Cp*Ru(bpy)Cl]: 87% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 8H: arom H), 7.05 (m, 2H: arom H), 5.87 (m, 1H, *J* = 10.1, 16.9, 7.6, 7.1 Hz: =C**H**), 5.41 (d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_E$), 5.31 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_Z$), 3.77 (dd, 1H, *J* =10.4, 3.3 Hz: C(O)CH_2C**H**Ph), 3.66 (AB, 2H: PhC**H**$_2$C(O)), 3.45 (dd, *J* =10.6, 17.4 Hz, 1H: C(O)C**H**$_2$), 3.22 (dd, *J* =3.5, 17.2 Hz, 1H: C(O)C**H**$_2$), 2.46(dd, *J* =7.6, 14.1 Hz, 1H: C**H**$_2$CH=), 2.42(dd, *J* =7.1, 13.9 Hz, 1H: C**H**$_2$CH=).

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.68 (**C**=O), 135.35 (Quat.), 133.17 (Quat.), 129.77-127.78 (Arom. **C**H; =**C**H), 123.75 (=**C**H_2), 115.46 (**C**N), 114.67 (**C**N), 51.03 (Ph**C**H_2C(O)), 46.37 (**C**HPh), 44.35 (C(O)**C**H_2), 43.23 (**C**$(CN)_2$), 40.68 (**C**H_2CH=).

FTIR ($CDCl_3$): ν_{max} 12251, 1720, 1454, 989.

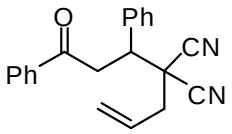
HRMS calcd for $C_{22}H_{20}N_2ONa$ [M+Na] 351.1473, found 351.1481.



allyl 3-oxo-3-phenylpropanoate
cw1159[8] (4:1)
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.97 (2H, d, *J*=8.0 Hz: arom H), 7.62 (1H, t, *J*=7.4 Hz: arom H), 7.51 (2H, t, *J*=7.0 Hz: arom H), 5.92 (1H, m: C**H**=), 5.33 (1H, d, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 5.25 (1H, d, *J*=10.4 Hz: CH=C**H**(*H*)$_Z$), 4.69 (2H, dd, *J*=5.7, 1.4 Hz: C**H**$_2$O), 4.06 (2H, d, *J*=1.8 Hz: C(O)C**H**$_2$) .

Enol form: 12.51 (1 H, s:O**H**), 7.80 (2H, d, *J*=6.9 Hz: arom H), 7.45 (2H, m: arom H), 6.02 (1H, m: C**H**=), 5.74 (1H, d, *J*=1.8 Hz: PhC(OH)=C**H**), 5.40 (1H, d, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 4.74 (2H, dd, *J*=5.7, 1.4 Hz: C**H**$_2$O).



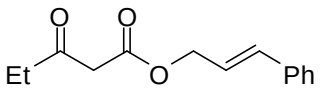
2-allyl-2-(3-oxo-1,3-diphenylpropyl)malononitrile
27e (cw1162)
colorless oil
[Cp*Ru(bpy)Cl]: 64% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.38 (10H: arom H), 5.95 (m, 1H, *J* = 10.1, 16.9, 7.1, 7.3 Hz: =C**H**), 5.44 (d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_E$), 5.36 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_Z$), 4.10-4.01 (m, 2H: overlapping C(O)CH$_2$C**H**Ph, C(O)C**H**$_2$), 3.70 (d, 1H, *J* = 14.4 Hz: C(O)C**H**$_2$), 2.55 (dd, *J* =7.3, 13.9 Hz, 1H: C**H**$_2$CH=), 2.43 (dd, *J* =7.1, 13.9 Hz, 1H: C**H**$_2$CH=).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.46 (**C**=O), 136.46 (Quat.), 135.92 (Quat.), 129.57-128.51 (overlapping Arom. **C**H; =**C**H), 123.80 (=**C**H$_2$), 115.69 (**C**N), 114.92 (**C**N), 46.53 (**C**HPh), 43.53 (**C**(CN)$_2$), 41.66 (C(O)**C**H$_2$), 40.83 (**C**H$_2$CH=).

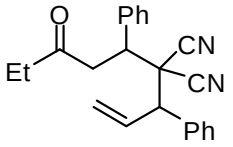
FTIR ($CDCl_3$): ν_{max} 3053, 2308, 1689, 1421, 989, 895.

HRMS calcd for $C_{21}H_{19}N_2O$ [M+H] 315.1497, found 315.1493.



cinnamyl 3-oxopentanoate
19a (cw1114)[9]
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.09 (0.06 H, s: C**H**(OH)=), 7.24 - 7.58 (5H, m: arom H), 6.71 (1H, d, *J*=16.0 Hz: PhC**H**=), 6.33(1H, m: =C**H**), 4.81 (2H, m: C**H**$_2$O), 3.52 (s, 2H: C(O)C**H**$_2$), 2.60 (2H, q, *J*=7.2 Hz: C**H**$_2$C(O)), 1.09 (3H, t, *J*=7.3 Hz: C**H**$_3$).



2-(3-oxo-1-phenylpentyl)-2-(1-phenylallyl)malononitrile
27f (cw1119)
colorless oil
[Cp*Ru(bpy)Cl]: 93% yield, dr = 1.8

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.50-7.28 (m, 10H: arom H), 6.42-6.33 (m, 1H, *J* = 16.9, 10.4, Hz: =C**H**), 5.53 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.23 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_Z$), 3.90 (dd, 1H, *J* =10.6, 3.3 Hz: C(O)CH$_2$C**H**Ph), 3.53-3.29 (m, 2H: overlapping C**H**Ph, C(O)C**H**$_2$), 3.18 (dd, *J* =13.9, 3.3 Hz, 1H: C(O)C**H**$_2$), 2.45 (m, 1H: C(O)C**H**$_2$), 2.21 (m, 1H: C(O)C**H**$_2$), 0.95(app. t, 3H: C(O)CH$_2$C**H**$_3$).

Minor diastereoisomer: δ 7.50-7.28 (m, 10H, arom H: overlapping minor/major isomer), 6.34-6.25 (m, 1H, =C**H:** overlapping minor/major isomer), 5.43 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.28 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_Z$), 3.76 (dd, 1H, *J* =10.6, 3.3 Hz: C(O)CH$_2$C**H**Ph), 3.53-3.29 (m, 2H: overlapping minor/major isomer C**H**Ph, C(O)C**H**$_2$), 3.05 (dd, *J* =13.9, 3.3 Hz, 1H: C(O)C**H**$_2$), 2.45 (m, 1H: overlapping minor/major isomer C(O)C**H**$_2$), 2.21 (m, 1H: overlapping minor/major isomer C(O)C**H**$_2$), 0.95(app. t, 3H: overlapping minor/major isomer C(O)CH$_2$C**H**$_3$);

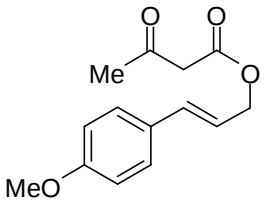
^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 206.84 (**C**=O), 137.30 (Quat.), 135.61 (Quat.), 132.61 (=**C**H), 129.51-128.92 (Arom. **C**H), 123.30 (=**C**H$_2$), 115.32 (**C**N), 114.42 (**C**N), 53.09 (**C**HPh), 48.84 (**C**(CN)$_2$), 45.85 (C(O)**C**H$_2$), 44.94 (C(O)CH$_2$**C**HPh), 37.22 (CH$_3$**C**H$_2$), 7.82 (**C**H$_3$).

Minor diastereoisomer: δ 206.84 (**C**=O: overlapping minor/major isomer), 136.22 (Quat.), 135.61 (Quat.), 134.09 (=**C**H), 129.51-128.92 (Arom. **C**H), 121.99 (=**C**H$_2$),

114.89(**C**N), 114.42 (**C**N), 54.35 (**C**HPh), 48.35 (**C**$(CN)_2$), 45.47 (C(O)**C**H_2), 44.65 (C(O)CH_2**C**HPh), 37.29 (CH_3**C**H_2), 7. 77 (**C**H_3).

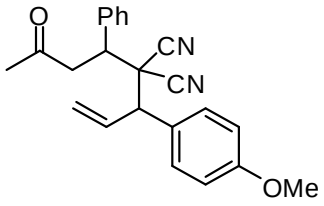
FTIR ($CDCl_3$): ν_{max} 2252, 1720, 1456, 991.

HRMS calcd for C23H22N2O1Na1 [M+Na] 365.2, found365.1.



(*E*)-3-(4-methoxyphenyl)allyl 3-oxobutanoate
cw1144[10]
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.35 (2H, d, *J*=8.8 Hz: arom H), 6.88 (2H, d, *J*=8.8 Hz: arom H), 6.64 (1H, d, *J*=16.0 Hz: =C**H**Ar), 6.17 (1H, dt, *J*=15.8, 6.7 Hz: C**H**=), 4.80 (2H, dd, *J*=6.7, 1.3 Hz: C$\mathbf{H}_2$O), 3.83 (2H, s: C(O)C$\mathbf{H}_2$), 2.30 (3H, s: C$\mathbf{H}_3$).



2-(1-(4-methoxyphenyl)allyl)-2-(3-oxo-1-phenylbutyl)malononitrile
27g (cw1149)
colorless oil
[Cp^*Ru(bpy)Cl]: 62% yield, dr = 1.6

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.50-7.21 (m, 5H: arom H), 6.94-6.88 (m, 4H: Arom. H), 6.38-6.23 (m, 1H, *J* = 16.9, 10.1, 9.1 Hz: =C**H**), 5.51 (d, 1H, *J* = 10.1 Hz: CH=C**H**$(H)_E$), 5.23 (d, 1H, *J* = 16.9 Hz: CH=C**H**$(H)_Z$), 3.81 (s, 3H: OC$\mathbf{H}_3$), 3.81-3.85(dd, 1H: overlapping C(O)CH_2C**H**Ph, OC$\mathbf{H}_3$), 3.48-3.31 (m, 2H: overlapping C**H**Ar, C(O)C$\mathbf{H}_2$), 3.20 (dd, *J* =17.2, 3.0 Hz, 1H: C(O)C$\mathbf{H}_2$), 2.09(s, 3H: C(O)C$\mathbf{H}_3$).

Minor diastereoisomer: δ 7.50-7.21 (m, 5H: arom H, overlapping minor/major isomer), 6.94-6.88 (m, 4H: Arom. H, overlapping minor/major isomer), 6.38-6.23 (m, 1H: =C**H,** overlapping minor/major isomer), 5.41 (d, 1H, *J* = 10.1 Hz: CH=C**H**$(H)_E$), 5.23 (d, 1H: CH=C**H**$(H)_Z$, overlapping minor/major isomer), 3.85 (s, 3H: OC$\mathbf{H}_3$), 3.71(dd, 1H, *J* =10.9, 3.0 Hz: C(O)CH_2C**H**Ph), 3.48-3.31 (m, 2H: overlapping

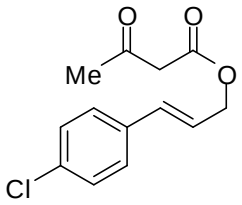
minor/major isomer: C**H**Ar, C(O)C**H**$_2$), 3.08 (dd, *J* =17.2, 3.0 Hz, 1H: C(O)C**H**$_2$), 2.05(s, 3H: C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 203.96 (**C**=O), 160.27 (Quat.), 135.74 (Quat.), 132.79 (=**C**H), 130.52-129.22 (Arom. **C**H), 122.67 (=**C**H$_2$), 114.82 (Arom. **C**H), 115.38 (**C**N), 114.82 (**C**N), 55.73 (O**C**H$_3$), 52.40 (**C**HAr), 49.17 (**C**(CN)$_2$), 47.01 (C(O)**C**H$_2$), 44.74 (**C**HPh), 31.12 (CH$_3$).

Minor diastereoisomer: δ 203.96 (**C**=O, overlapping minor/major isomer), 136.20 (Quat.), 134.26 (=**C**H), 130.52-129.22 (Arom. **C**H, overlapping minor/major isomer), 127.41 (Quat.), 121.59 (=**C**H$_2$), 114.82 (Arom. **C**H, overlapping minor/major isomer), 114.94 (**C**N), 114.50 (**C**N), 55.67 (O**C**H$_3$), 53.61 (**C**HAr), 48.58 (**C**(CN)$_2$), 46.58 (C(O)**C**H$_2$), 44.51 (**C**HPh), 31.17 (CH$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 2247, 1724, 1253.

HRMS calcd for $C_{23}H_{22}N_2O_2Na$ [M+Na] 381.1579, found 381.1556.

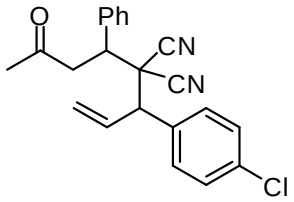


(*E*)-3-(4-chlorophenyl)allyl 3-oxobutanoate

19b (cw1145)[11]

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.04 (0.1 H, s: C**H**(OH)=), 7.32 (4H, m: arom H), 6.63 (3 H, d, *J*=15.9, 1.1 Hz: =C**H**Ar), 6.27 (5 H, dt, *J*=15.9, 6.5 Hz: C**H**=), 4.81 (2H, dd, *J*=6.4, 1.3 Hz: C**H**$_2$O), 3.53 (2H, s: C(O)C**H**$_2$), 2.31 (3H, s: C**H**$_3$).



2-(1-(4-chlorophenyl)allyl)-2-(3-oxo-1-phenylbutyl)malononitrile

27h (cw1155)

colorless oil

[Cp^*Ru(bpy)Cl]: 62% yield, dr = 1.8

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.50-7.22 (m, 9H: arom H), 6.31 (m, 1H, *J* = 16.7, 10.4, 9.1 Hz: =C**H**), 5.55 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.21 (d, 1H, *J* = 16.7 Hz: CH=C**H**(*H*)$_Z$), 3.88 (dd, *J* =10.6, 3.0 Hz, 1H: C(O)CH$_2$C**H**Ph), 3.44-3.34 (m, 2H: overlapping C**H**Ar, C(O)C**H**$_2$), 3.21 (dd, *J* =17.4, 3.3 Hz, 1H: C(O)C**H**$_2$), 2.10 (s, 3H: C(O)C**H**$_3$).

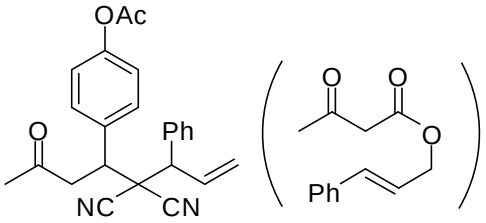
Minor diastereoisomer: δ 7.43-7.22 (m, 9H: arom H), 6.24 (m, 1H, *J* = 16.7, 10.4, 9.1 Hz: =C**H**), 5.44 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.26 (d, 1H, *J* = 16.7 Hz: CH=C**H**(*H*)$_Z$), 3.69 (dd, *J* =10.6, 3.0 Hz, 1H: C(O)CH$_2$C**H**Ph), 3.49 (d, 1H, *J* = 8.8 Hz: C**H**Ar), 3.35 (dd, *J* =17.2, 10.4 Hz, 1H: C(O)C**H**$_2$), 3.10 (dd, *J* =16.9, 3.0 Hz, 1H: C(O)C**H**$_2$), 2.07 (s, 3H: C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 203.83 (**C**=O), 135.86 (Quat.), 135.42 (Quat.), 131.98 (=**C**H), 130.30 (Arom. **C**H), 129.54 (Arom. **C**H), 123.56 (=**C**H$_2$), 115.06 (**C**N), 114.25 (**C**N), 52.29 (**C**HAr), 48.65 (**C**(CN)$_2$), 47.17 (C(O)**C**H$_2$), 44.79 (**C**HPh), 31.12 (CH$_3$).

Minor diastereoisomer: δ 203.78 (**C**=O), 135.91 (Quat.), 135.39 (Quat.), 133.56 (=**C**H), 130.70-128.22 (Arom. **C**H), 122.39 (=**C**H$_2$), 115.14 (**C**N), 114.63 (**C**N), 53.57 (**C**HAr), 48.21 (**C**(CN)$_2$), 46.62 (C(O)**C**H$_2$), 44.53 (**C**HPh), 31.19 (CH$_3$).

FTIR ($CDCl_3$): ν_{max} 2253, 1726, 1425, 990, 912.

HRMS calcd for $C_{21}H_{20}NOCl$ [M+H-HCN] 337.1, found 337.0.

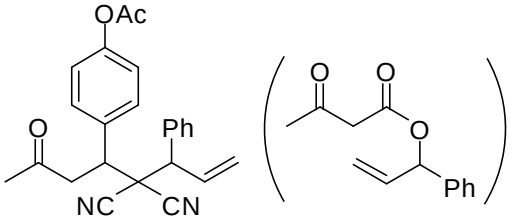


4-(5',5''-dicyano-2-oxo-6-phenyloct-7-en-4-yl)phenyl acetate

27i (cw1111)

colorless oil

[Cp*Ru(bpy)Cl]: 92% yield, dr = 2.7



4-(5',5''-dicyano-2-oxo-6-phenyloct-7-en-4-yl)phenyl acetate

27i (cw1139)

colorless oil

[Cp*Ru(bpy)Cl]: 76% yield, dr = 4.5

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.51-7.09 (10H: arom H), 6.40-6.23 (m, 1H, *J* = 10.4, 17.4 Hz: =C**H**), 5.53 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.25 (d, 1H, *J* = 17.4 Hz: CH=C**H**(*H*)$_Z$), 3.89 (dd, 1H, *J* =3.0, 10.4 Hz: C(O)CH$_2$C**H**), 3.49-3.27 (m, 2H: overlapping C**H**Ph, C(O)C**H**$_2$), 3.22 (dd, *J* =3.0, 17.4 Hz, 1H: C(O)C**H**$_2$), 2.34 (s, 3H: OC(O)C**H**$_3$), 2.11(s, 3H: C(O)C**H**$_3$).

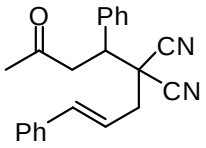
Minor diastereoisomer: δ 7.51-7.09 (10H: arom H, overlapping minor/major isomer), 6.40-6.23 (m, 1H: =C**H,** overlapping minor/major isomer), 5.42 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_E$), 5.25 (d, 1H, *J* = 17.4 Hz: CH=C**H**(*H*)$_Z$, overlapping minor/major isomer), 3.74 (dd, 1H, *J* =3.0, 10.4 Hz: C(O)CH$_2$C**H**), 3.49-3.27 (m, 2H: overlapping minor/major isomer C**H**Ph, C(O)C**H**$_2$), 3.11 (dd, *J* =3.0, 17.4 Hz, 1H: C(O)C**H**$_2$), 2.32 (s, 3H: OC(O)C**H**$_3$), 2.07 (s, 3H: C(O)C**H**$_3$);

^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 203.05 (**C**=O), 169.46 (O**C**=O), 151.49 (Quat.), 137.12 (Quat.), 132.45 (=**C**H), 133.11 (Quat.), 129.57-129.91 (Arom. **C**H), 122.59 (overlapping =**C**H$_2$, Arom. **C**H), 115.17 (**C**N), 114.30 (**C**N), 53.07 (**C**HPh), 48.77 (**C**(CN)$_2$), 47.16 (C(O)**C**H$_2$), 44.15 (**C**HAr), 31.02 (**C**H$_3$C(O)), 21.62 (OC(O)**C**H$_3$).

Minor diastereoisomer: δ 203.05 (**C**=O, overlapping minor/major isomer), 169.46 (O**C**=O, overlapping minor/major isomer), 135.40 (Quat.), 134.06 (=**C**H), 133.52 (Quat.), 133.11 (Quat.), 130.63 (Arom. **C**H), 129.57-129.91 (Arom. **C**H, overlapping minor/major isomer), 122.59 (=**C**H_2, Arom. **C**H, overlapping minor/major isomer), 115.17/114.30 (**C**N, overlapping minor/major isomer), 54.27 (**C**HPh), 48.16 (**C**$(CN)_2$), 46.87 (C(O)**C**H_2), 43.82 (**C**HAr), 31.07 (**C**H_3C(O)), 21.62 (OC(O)**C**H_3, overlapping minor/major isomer).

FTIR ($CDCl_3$): ν_{max} 3053, 2305, 1769, 1724, 1421, 1205, 895.

HRMS calcd for $C_{24}H_{22}N_2O_3Na$ [M+Na] 409.1528, found 409.1523.



2-cinnamyl-2-(3-oxo-1-phenylbutyl)malononitrile

30b (cw1124)

colorless oil

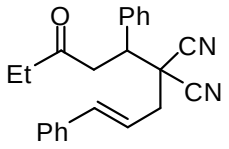
$Pd(PPh_3)_4$: 80% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.33 (m, 10H: arom H), 6.65 (d, 1H, *J* = 15.7 Hz: =C**H**Ph), 6.26 (m, 1H, *J* = 15.7, 7.6, 7.3 Hz: CH_2C**H**=), 3.85 (dd, 1H, *J* =10.4, 3.5 Hz: C(O)CH_2C**H**Ph), 3.48 (dd, *J* = 17.4, 10.4 Hz, 1H: C(O)C**H**$_2$), 3.26 (dd, *J* = 17.4, 3.5 Hz, 1H: C(O)C**H**$_2$), 2.73 (dd, *J* = 7.6, 13.9 Hz, 1H: C**H**$_2$CH=), 2.60 (dd, *J* = 7.3, 13.9 Hz, 1H: C**H**$_2$CH=), 2.15 (s, 3H: C(O)C**H**$_3$);

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.96 (**C**=O), 137.99 (=**C**HPh), 136.19 (Quat.), 136.19 (Quat.), 129.57 (Arom. **C**H), 129.50 (Arom. **C**H), 129.46 (Arom. **C**H), 129.17 (Arom. **C**H), 128.90 (Arom. **C**H), 127.14 (Arom. **C**H), 122.07 (CH_2**C**H=), 115.78 (**C**N), 115.00 (**C**N), 46.35 (**C**HPh), 46.20 (C(O)**C**H_2CHPh), 43.88 (**C**$(CN)_2$), 40.26 (**C**H_2CH=), 30.87 (CH_3).

FTIR ($CDCl_3$): ν_{max} 2248, 1724, 1456, 968.

HRMS calcd for $C_{44}H_{40}N_4O_2Na$ [2M+Na] 679.3049, found 679.3074.



2-cinnamyl-2-(3-oxo-1-phenylpentyl)malononitrile

30c (cw1156)

colorless oil

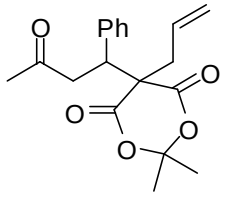
$Pd(PPh_3)_4$: 88% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.31 (m, 10H: arom H), 6.60 (d, 1H, *J* = 15.7 Hz: =C**H**Ph), 6.21 (m, 1H, *J* = 15.7,7.8,7.3 Hz: C**H**=CHPh), 3.86 (dd, 1H, *J* =10.1, 3.5 Hz: C(O)CH_2C**H**Ph), 3.42 (dd, 1H, *J* =10.1, 17.1 Hz: EtC(O)C**H**$_2$), 3.20 (dd, 1H, *J* =3.5, 17.1 Hz: EtC(O)C**H**$_2$), 2.66 (dd, *J* =13.9, 7.8 Hz, 1H:C**H**$_2$CH=), 2.58-2.47 (m, 2H: overlapping C**H**$_2$CH=, C**H**$_2$C(O)), 2.31 (q, 1H, *J* =7.3 Hz: C**H**$_2$C(O)), 0.95 (t, 3H, *J* =7.3 Hz: C(O)CH_2C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 206.77 (**C**=O), 138.27 (=**C**HPh), 136.15 (Quat.), 135.82 (Quat.), 129.64-128.87 (Arom. **C**H), 127.12 (Arom. **C**H), 119.53 (**C**H=CHPh), 115.67 (**C**N), 114.90 (**C**N), 46.47 (**C**HPh), 45.30 (EtC(O)**C**H_2) 43.68 (**C**$(CN)_2$), 40.22 (**C**H_2CH=), 37.20 (**C**H_2C(O)), 7.87 (**C**H_3).

FTIR ($CDCl_3$): ν_{max} 2249, 1720, 1456, 968.

HRMS calcd for $C_{23}H_{23}N_2O$ [M+H] 343.1810, found 343.1830.



5-allyl-2',2"-dimethyl-5-(3-oxo-1-phenylbutyl)-1,3-dioxane-4,6-dione

31a (cw1120)

colorless oil

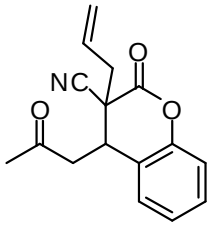
[Cp*Ru(bpy)Cl]: 51% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 3H: arom H), 7.19 (d, *J* = 6.8 Hz, 2H: arom H), 5.74-5.64 (m, 1H, *J* = 12.9, 5.1, 12.6 Hz: =C**H**), 5.25 (d, 1H, *J* = 12.9 Hz: CH=C**H**(*H*)$_Z$), 5.22 (d, 1H, *J* = 5.1 Hz: CH=C**H**(*H*)$_E$), 4.05 (dd, 1H, *J* =8.8, 5.3 Hz: C(O)CH_2C**H**Ph), 3.35 (app t, 2H: C(O)C**H**$_2$), 2.89 (dd, *J* =7.8, 12.6 Hz, 1H: C**H**$_2$CH=), 2.77 (dd, *J* =7.3, 12.6 Hz, 1H: C**H**$_2$CH=), 2.10 (s, 3H: C(O)C**H**$_3$), 1.52 (s, 3H: C**H**$_3$), 0.71 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 206.01 (**C**=O), 168.46 (O**C**=O) 167.80 (O**C**=O) 139.41 (Quat.), 131.70 (=**C**H), 129.59 (Arom. **C**H), 129.38 (Arom. **C**H), 128.57 (Arom. **C**H), 121.99 (=**C**H_2), 106.64 (**C**$(CH_3)_2$), 59.89 (**C**$(CO_2R)_2$), 47.89 (**C**HPh), 43.91 (C(O)**C**H_2), 41.42 (**C**H_2CH=), 30.91/30.82 (overlapping C(O)**C**H_3 with **C**H_3), 28.26 (**C**H_3).

FTIR ($CDCl_3$): ν_{max} 3063, 1765, 1732, 1456.

HRMS calcd for $C_{19}H_{22}O_5Na$ [M+Na] 353.1365, found 353.1347.



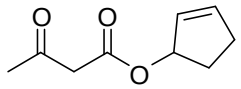
3-allyl-2-oxo-4-(2-oxopropyl)chroman-3-carbonitrile
31b (cw1193)
colorless oil
[Cp^*Ru(bpy)Cl]: 45% yield, dr = 12

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 2H: arom H), 7.18 (app. t, 1H: arom H), 7.09 (app. d, 1H: arom H), 5.85 (m, 1H, *J* = 10.1, 16.9 Hz: =C**H**), 5.33 (d, 1H, *J* = 10.1 Hz, CH=C**H**$(H)_E$), 5.10 (d, 1H, *J* = 16.9 Hz: CH=C**H**$(H)_Z$), 3.80 (dd, 1H, *J* = 6.6, 3.0 Hz: C**H**), 3.16 (dd, 1H, *J* =17.9, 2.8 Hz: C(O)C**H**$_2$), 2.83 (dd, 1H, *J* =17.9, 9.6 Hz,: C(O)C**H**$_2$), 2.59 (dd, *J* =6.6, 14.1 Hz, 1H: C**H**$_2$CH=), 2.38 (dd, 1H, *J* =8.1, 13.9 Hz: C**H**$_2$CH=), 2.11 (3H: C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 206.35 (**C**=O), 162.95 (O**C**=O), 149.94 (Quat.), 130.31 (Arom. **C**H), 129.04 (=**C**H), 126.11 (Arom. **C**H), 123.16 (=**C**H_2), 121.51 (Quat.), 117.25 (Arom. **C**H), 116.84 (**C**N), 49.70 (*t*-**C**(CN)(CO_2)), 47.03 (C(O)**C**H_2), 38.38 (overlapping **C**H_2CH=, **C**HCH_2CO), 30.83 (**C**H_3).

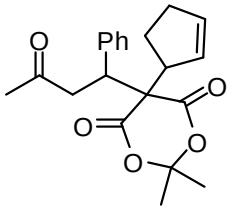
FTIR ($CDCl_3$): ν_{max} 2250, 1780, 1726, 912.

HRMS calcd for $C_{16}H_{15}NO_3Na$ [M+Na] 292.0950, found 292.0946.



cyclopent-2-enyl 3-oxobutanoate
cw1135
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.15 (1H, m: OC**H**), 5.85 (1H, dd, *J*=3.3, 2.2 Hz: C**H**=), 5.78 (1H, m: =C**H**CH_2), 3.44 (2H, s: C(O)C**H**$_2$), 2.53 (1H, m: C**H**$_2$), 2.33 (4H, m: overlapping C**H**$_3$, C**H**$_2$), 1.87 (1H, m: C**H**$_2$), 1.73 (1H, m: C**H**$_2$).



5-(cyclopent-2-enyl)-2,2-dimethyl-5-(3-oxo-1-phenylbutyl)-1,3-dioxane-4,6-dione
31c (cw1123)
colorless oil
[Cp*Ru(bpy)Cl]: 65% yield, dr = 5.5

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.31 (m, 2H: arom H), 7.25 (m, 2H: arom H), 7.24 (m, 1H: arom H), 5.97 (m, 1H, =C**H**), 5.51 (m, 1H, =C**H**), 4.26 (dd, 1H, *J* =11.6, 3.0 Hz: C**H**Ph), 3.77-3.63 (m, 2H: overlapping C**H**CH=CH, C(O)C**H**$_2$), 3.14 (dd, *J* =2.0, 17.4 Hz ,1H: C(O)C**H**$_2$), 2.56 (m, 1H: C**H**$_2$CHCH=CH), 2.46 (m, 1H: C**H**$_2$CH=), 2.37 (m, 1H: C**H**$_2$CH=), 2.08 (m, 1H: C**H**$_2$CHCH=CH), 2.08 (s, 3H: C(O)C**H**$_3$), 1.54 (s, 3H: C**H**$_3$), 0.50 (s, 3H: C**H**$_3$);

Minor diastereoisomer: δ 7.31-7.24 (m, 5H: arom H), 5.97 (m, 1H: =C**H,** overlapping minor/major isomer), 5.36 (m, 1H, =C**H**), 4.26 (dd, 1H: C**H**Ph, overlapping minor/major isomer), 3.77-3.63 (m, 2H: overlapping minor/major isomer C**H**CH=CH, C(O)C**H**$_2$), 3.14 (1H: C(O)C**H**$_2$, overlapping minor/major isomer), 2.56 (1H: C**H**$_2$CHCH=CH, overlapping minor/major isomer), 2.46 (1H: C**H**$_2$CH=, overlapping minor/major isomer), 2.37 (1H: C**H**$_2$CH=, overlapping minor/major isomer), 2.08 (1H: C**H**$_2$CHCH=CH, overlapping minor/major isomer), 2.08 (s, 3H: C(O)C**H**$_3$, overlapping minor/major isomer), 1.54 (s, 3H: C**H**$_3$, overlapping minor/major isomer), 0.50 (s, 3H: C**H**$_3$, overlapping minor/major isomer).

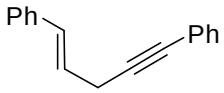
^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 206.31 (**C**=O), 169.40 (O**C**=O) 167.72 (O**C**=O), 139.78 (Quat.), 136.36 (=**C**H: δ=5.97ppm), 130.14 (Arom. **C**H), 129.46 (Arom. **C**H), 128.37 (=**C**H: δ=5.51ppm), 106.27 (**C**$(CH_3)_2$), 62.11 (**C**$(CO_2R)_2$), 55.19 (**C**HCH=CH), 44.27 (**C**HPh), 43.87(C(O)**C**H_2), 32.73 (**C**H_2CH=:

δ= 2.37ppm), 29.61 (**C**H_3), 29.37 (**C**H_3), 29.16 (**C**H_3), 23.85 (**C**H_2CHCH=CH: δ= 2.08ppm).

Minor diastereoisomer: δ 206.31 (**C**=O, overlapping minor/major isomer), 168.65 (O**C**=O) 166.77 (O**C**=O), 140.70 (Quat.), 134.36 (=**C**H: δ=5.97ppm), 130.14, 129.46 (Arom. **C**H, overlapping minor/major isomer), 128.37 (=**C**H: δ=5.51ppm, overlapping minor/major isomer), 106.51 (**C**$(CH_3)_2$), 62.48 (**C**$(CO_2R)_2$), 55.19 (**C**HCH=CH, overlapping minor/major isomer), 44.78 (**C**HPh), 43.69 (C(O)**C**H_2), 32.09 (**C**H_2CH=: δ=2.46 ppm), 29.61, 29.37, 29.16 (**C**H_3, overlapping minor/major isomer), 27.63 (**C**H_2CHCH=CH, δ=2.56 ppm).

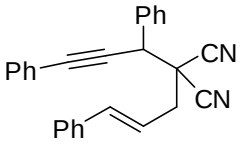
FTIR ($CDCl_3$): ν_{max} 3063, 1765, 1732, 1456, 945.

HRMS calcd for $C_{21}H_{24}N_2O_5Na$ [M+Na] 379.1521, found 379.1511.



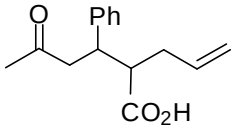
(*E*)-pent-1-en-4-yne-1,5-diyldibenzene
34b[13] (cw1212)
colorless oil
40% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.51 (m, 5H: arom H), 6.75 (d, 1 H, *J*=15.7 Hz: =C**H**Ph), 6.29 (dt, 1 H, *J* =6.0, 16.0 Hz: C**H**CH_2), 3.41 (d, 2 H, *J*=4.0 Hz: C**H**$_2$).



2-cinnamyl-2-(1,3-diphenylprop-2-ynyl)malononitrile
34c (cw1212)
colorless oil
40% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.66 (m, 10H: arom H), 6.80 (d, 1 H, *J*=15.7 Hz: =C**H**Ph), 6.29 (ddd, 1 H, *J* =15.4, 7.6, 7.5 Hz: C**H**CH_2), 4.39 (s, 1 H: C**H**Ph), 3.14 (t, 1H, *J*=8.1 Hz: C**H**$_2$).



2-allyl-5-oxo-3-phenylhexanoic acid
36a (cw1177)
colorless oil
80% yield, dr = 1.5

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ 7.33 (m, 2H: arom H), δ 7.26 (m, 3H: arom H), δ 5.70 (m, 1H, *J* = 7.3 Hz: =C**H**), 4.97 (app s, 1H, CH=C**H**(*H*)$_Z$), 4.94 (d, 1H, *J* = 7.3 Hz: CH=C**H**(*H*)$_E$), 3.33 (td, 1H, *J* =10.4, 3.8 Hz: C(O)CH$_2$C**H**Ph), 2.98 (dd, 1H, *J* =10.4, 16.4Hz: C(O)C**H**$_2$), 2.77 (dd, 1H, *J* =3.8, 16.4 Hz: C(O)C**H**$_2$), 2.67 (td, *J* =4.1, 1H, 10.1 Hz: C**H**CO$_2$H), 2.10 (m, 1H: overlapping H_2O, C**H**$_2$CH=), 1.97 (3H: overlapping CD_3CN, C**H**$_2$CH=), 1.97 (3H: overlapping CD_3CN, C(O)C**H**$_3$).

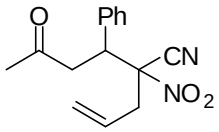
Minor diastereoisomer: δ 7.35-7.23 (m, 5H: arom H, overlapping minor/major isomer), δ 5.80 (m, 1H, *J* = 17.2, 9.9 Hz: =C**H**), 5.06 (d, 1H, *J* = 17.2 Hz, CH=C**H**(*H*)$_Z$), 5.04 (d, 1H, *J* = 9.9 Hz: CH=C**H**(*H*)$_E$), 3.42 (td, 1H, *J* =9.2, 4.8 Hz: C(O)CH$_2$C**H**Ph), 3.03-2.88 (m, 1H: C(O)C**H**$_2$, overlapping minor/major isomer), 2.80-2.65 (m, 2H: overlapping minor/major isomer C(O)C**H**$_2$, C**H**CO$_2$H), 2.32 (m, 2H: overlapping H_2O, C**H**$_2$CH=), 1.97 (3H: overlapping minor/major isomer CD_3CN, C(O)C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) Major diastereoisomer: δ 206.26 (**C**=O), 174.34 (HO**C**=O), 141.41 (Quat.), 135.03 (=**C**H), 128.07 (Arom. **C**H), 126.47 (Arom. **C**H), 115.82 (=**C**H$_2$), 50.31 (**C**HCO$_2$H), 46.96 (C(O)**C**H$_2$), 42.52 (**C**HPh), 34.20 (**C**H$_2$CH=), 29.26 (**C**H$_3$).

Minor diastereoisomer: δ 206.85 (**C**=O), 174.97 (HO**C**=O), 142.01 (Quat.), 135.59 (=**C**H), 128.22 (Arom. **C**H, overlapping minor/major isomer), 126.62 (Arom. **C**H), 116.24 (=**C**H$_2$, overlapping minor/major isomer), 50.29 (**C**HCO$_2$H), 45.98 (C(O)**C**H$_2$), 42.12 (**C**HPh), 33.85 (**C**H$_2$CH=), 29.53 (**C**H$_3$, overlapping minor/major isomer).

FTIR ($CDCl_3$): ν_{max} 1745, 1711.

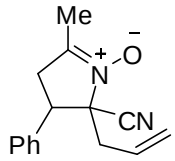
HRMS calcd for $C_{15}H_{18}O_3Na$ [M+Na] 269.1154, found 269.1154.



2-allyl-2-nitro-5-oxo-3-phenylhexanenitrile
37b (cw2064)
colorless oil
$Pd(PPh_3)_4$, 56% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.34 (m, 5H: arom H), 5.78 (m, 1H: =C**H**), 5.35 (dd, 1H, *J*=5.0, 0.7 Hz: CH=C**H**(*H*)$_Z$), 5.35 (dd, 1H, *J*=11.8, 0.9 Hz: CH=C**H**(*H*)$_E$), 4.16 (dd, 1H, *J*=8.9, 4.3 Hz: C(O)CH_2C**H**Ph), 3.29 (dd, 1H, *J*=17.7, 8.9 Hz: C(O)C**H**$_2$), 3.09 (m, 2H: overlapping C**H**$_2$CH=, C(O)C**H**$_2$), 2.83 (dd, 1H, *J*=14.5, 6.5 Hz: C**H**$_2$CH=), 2.14 (s, 3H: C(O)C**H**$_3$).

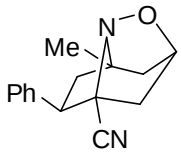
^{13}C NMR (100 MHz, $CDCl_3$) δ 203.95 (**C**=O), 136.15 (Quat.), 129.54 (=**C**H), 129.54 (Arom. **C**H), 123.36 (=**C**H_2), 115.66 (**C**N), 114.91 (**C**N), 46.25 (**C**HPh), 46.10 (C(O)**C**H_2), 43.52 (**C**$(CN)_2$), 40.73 (**C**H_2CH=), 30.86 (CH_3).



2-allyl-2-cyano-5-methyl-3-phenyl-3,4-dihydro-2*H*-pyrrole 1-oxide
37c (cw2083)
colorless oil
79% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.42 (m, 3H: arom H), 7.34 (d, 2H, *J*=8.0 Hz: arom H), 5.76 (m, 1H: =C**H**), 5.42 (m, 2H: C**H**$_2$=), 3.74 (t, 1H, *J*=8.0 Hz: C**H**$_2$), 3.11 (m, 3H: overlapping C**H**$_2$CH=, C**H**Ph and C**H**$_2$), 2.87 (dd, 1H, *J*=14.2, 8.1 Hz: C**H**$_2$CH=), 2.23 (s, 3H: C**H**$_3$).

^{13}C NMR (101MHz, $CDCl_3$) δ ppm 145.7 (**C**=N), 136.2 (Quat. arom **C**), 129.8 (=**C**H), 129.6 (Arom. **C**H), 129.3 (Arom. **C**H), 128.9 (Arom. **C**H), 123.3 (=**C**H_2), 116.0 (**C**N), 79.0 (Quat. **C**), 44.6 (**C**H_2), 39.7 (**C**HPh), 37.9 (**C**H_2CH=), 13.8 (**C**H_3).



37d (cw2097)
brown solid
35% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.39-7.40 (m, 4H: arom H), 7.33 (ddd, 1H, *J*=4.9, 3.4, 2.4 Hz: arom H), 4.98 (t, 1H, *J*=4.9 Hz: OC**H**), 3.57 (dd, 1H, *J*=10.1, 5.6 Hz: C**H**Ph), 2.73 (m, 2H: overlapping C**H**$_2$CH, C**H**$_2$CHPh), 2.08 (dd, 1H, *J*=14.2, 5.6 Hz: C**H**$_2$CHPh), 1.97 (m, 2H: overlapping C**H**$_2$C(CN)N, C**H**$_2$CH), 1.64 (d, 1H, *J*=11.9 Hz: C**H**$_2$C(CN)N), 1.47 (s, 3H: C**H**$_3$).

^{13}C NMR (101MHz, $CDCl_3$) δ ppm 142.8 (Quat. **C**), 129.3 (Arom. **C**H), 128.6 (Arom. **C**H), 128.2 (Arom. **C**H), 120.7 (**C**N), 81.0 (O**C**H), 72.9 (Quat. **C**N(CN)), 71.5 (Quat. **C**N(OCH)), 50.5 (**C**HPh), 49.8 (**C**H$_2$CH), 48.4 (**C**H$_2$C(CN)N), 44.4 (**C**H$_2$CHPh), 28.2 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3067, 2976, 2241, 1495, 1456, 1292, 883.

HRMS calcd for $C_{15}H_{17}N_2O$ [M+] 241.1341, found 241.1341.

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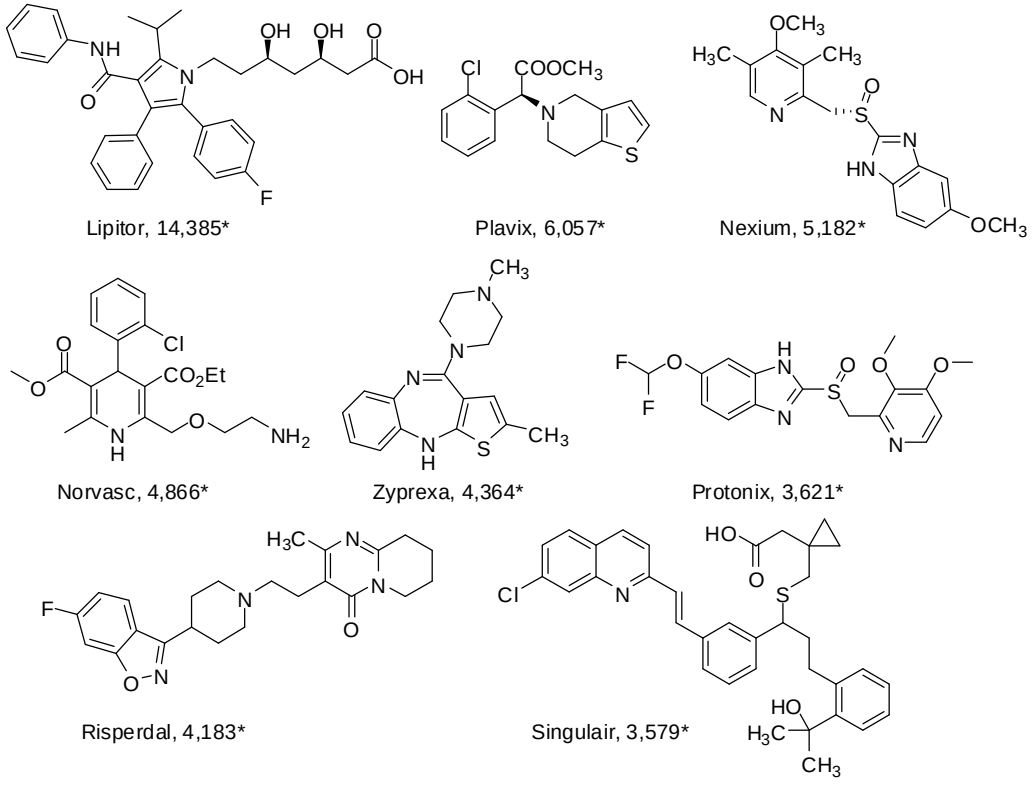
Chapter 2

The Synthesis of Nitrogen-Containing Heterocycles *via* the Palladium-Catalyzed Decarboxylative Allylation

2.1 Importance of Nitrogen Heterocycles in the Pharmaceutical Industry

Heterocycles are structural motifs found in 68% of drugs in the clinical stage or on the market, and seven of the top ten selling drugs are *N*-heterocycles (Figure 1).[1, 2] These structural components are also found in biologically active natural products.[1] To match the increasing interest in *N*-containing heterocycles, many methods have been developed for efficient synthesis of those important heterocycles, on gram to ton scale for industrial production.[2, 3]

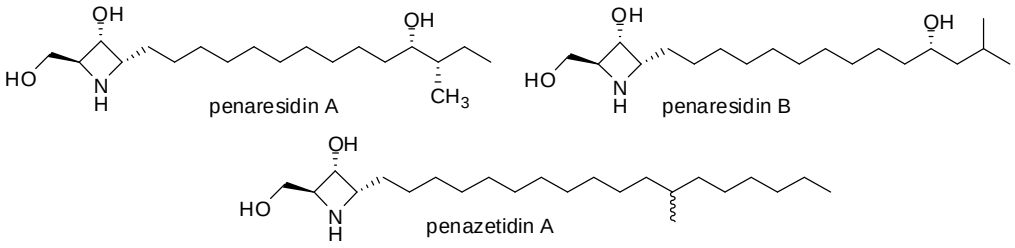
Figure 1 *Structures of top-selling drugs*



Source: MedAdNews 200 - World's Best-Selling Medicines, MedAdNews, July 2007
* unit in millions USD

An interesting subclass of *N*-heterocycles is the four-membered azetidine alkaloids, which have not drawn a lot of attention as compared to the analogous aziridine, pyrrolidine and piperidine alkaloids. The reason partially resides in the fact that there are not many natural products reported to include the azetidine ring structure. Nevertheless, azetidine rings do show up as the structural motifs of some pharmaceuticals and agrochemicals due to their interesting biological activities. For example, sphingosine derivatives penaresidin A and B isolated from a marine sponge exhibit potent actomyosin ATPase-activating activity, while penazetidin A is found to be a protein kinase C inhibitor (Figure 2).[4, 5] All these compounds feature a hydroxyl azetidine ring and their syntheses have been achieved by several synthetic groups.[6-11]

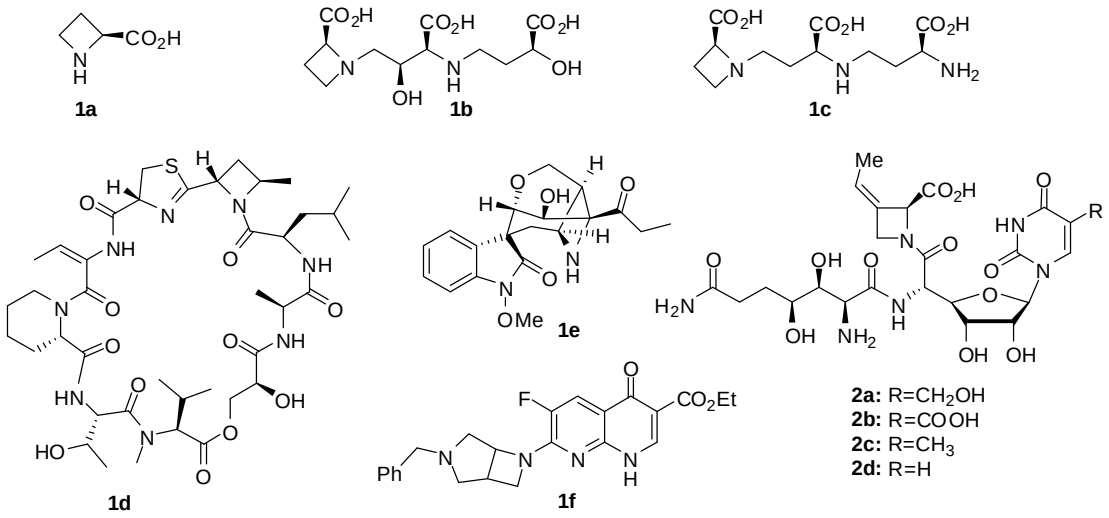
Figure 2 *Sphingosine type azetidine alkaloids isolated from marine sponge*



Some other representative examples are shown in Figure 3. Enantiopure *L*-azetidine carboxylic acid (*L*-Aze) **1a** was isolated from *convallaria majalis* plants and serves an potential building block for a variety of molecules.[12] Mugineic acid (**1b**), excreted from the roof of barley, is a typical phytosiderophore, promoting the absorption and transportation of iron in plants.[13] Nicotianamine **1c**, present in "soy

sauce" was identified as an inhibitor of angiotensin I-converting enzyme (ACE).[14] Vioporlide A **1d**, isolated from *cystobaxter violoceus* displays interesting antifungal activity.[15] Due to its complex and challenging ring structure, gelsemoxonie **1e** has been a synthetic target ever since it was separated from *gelemium elegants.*[16] Furthermore, gelsemoxonie **1e** has shown potent analgesic and antispasmodic activity.[17] Another interesting family of azetidine alkaloids are the polyxins **2a**-**2d**, which are present in cultures of s*treptomyces cacaoi var. asoenisis* and exhibits antifungal activity.[18]

Figure 3 *Natural products bearing an azetidine ring*



In addition, azetidine alkaloids could become the target of medicinal chemistry studies in which *N*-heterocycles are frequently studied. For example, a neuronal nicotinic acetylcholine receptor (nAChR) inhibitor ABT-594 was identified in the

SAR study of morphine-related non-opioid drug (-)-epibatidine with similar potency (Figure 4).[19, 20] More importantly, ABT-594 did not appear to cause opioid-related physical dependence or opioid analgesic activity, which should motivate further studies of azetidine analogs.

Figure 4 *Synthetic azetidine ABT-594 as analog of natural (-)-epibatidine*

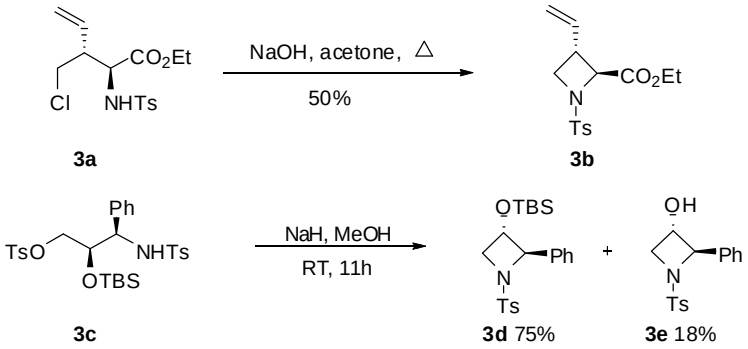
ABT-594 (-)-epibatidine

2.2 Overview of Azetidine Synthesis

2.2.1 Azetidine Ring Syntheses from 1,3 –Amino Halides

A traditional way for azetidine ring synthesis is intramolecular cyclization of amines bearing a good leaving group at the γ-position, for example γ–chloroamines **3a**, as shown in Scheme 1.[21, 22] Other leaving groups were also tested in this context, including: bromo, iodo, tosylate, mesylate and triflate groups. It was found that, due to slow kinetics (unfavorable enthalpy of activation) of four-membered ring closure, those transformations were generally very slow even when treated with a strong base at higher temperatures.[23] The best combination was shown by Shioiri, in which tosylamide **3c** with a tosylate leaving group was utilized as the reactant.[24] The intramolecular S_N2 substitution yields the azetidine product **3d** and **3e** in combined 93% yield with the correct stereochemistry.

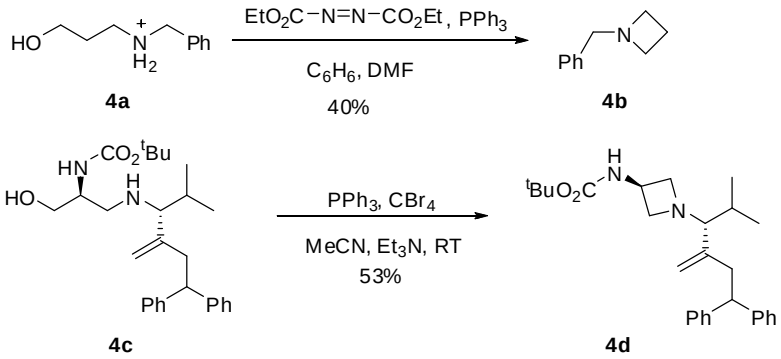
Scheme 1 *Intramolecular Ring closure of 1,3–amino halides*



2.2.2 Azetidine Ring Syntheses from 1,3–Amino Alcohols

Azetidine rings can also be synthesized from 1,3–amino alcohols under Mitsunobu-type reaction conditions, in which stoichiometric amount of PPh_3 is used in the presence of an oxidant such as DEAD, Br_2 or CBr_4 (Scheme 2).[25, 26] Even though the reactions can be carried out under mild conditions, the yields of azetidine products **4b** and **4d** are moderate.[27, 28] Furthermore, in addition to the poor atom economy of these reactions, the phosphine oxide byproducts are notorious for complicating product purification.

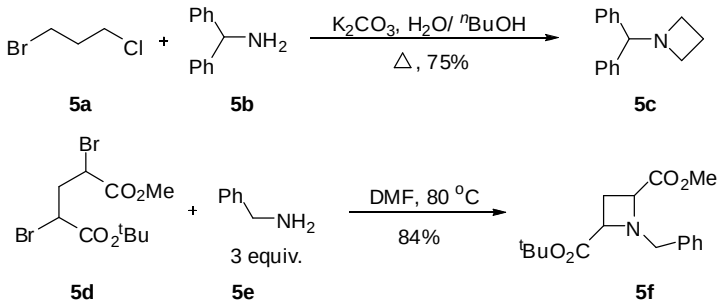
Scheme 2 *Intramolecular Ring closure of 1,3–amino alcohols*



2.2.3 One Pot Azetidine Ring Syntheses from via 1,3-Dielectrophiles

For the intramolecular azetidine ring closure reactions, secondary amines are used to avoid the byproducts of competitive dialkylation. However, by carefully controlling the reaction conditions, the cyclized azetidine ring product **5c** was produced *via* dialkylation of primary amine **5b** in 75% yield as shown in Scheme 3.[29] One thing to note here is that this transformation could be carried out on kilogram scale. Dibromoelectrophile **5d** was also used to synthesize the azetidine product **5f**. However the reaction conditions need to be carefully controlled to avoid competing reactions.[30]

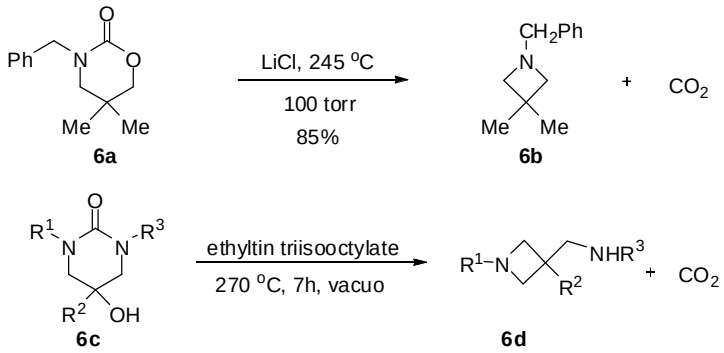
Scheme 3 *Intramolecular ring closure of 1,3-dielectrophiles with primary amines*



2.2.4 Azetidine Ring Syntheses via Ring Contraction

Lastly, decarboxylative ring contraction of carbamate **6a** yielded azetidine **6b** in 85% yield at high temperature and pressure (Scheme 4).[31] Similarly, the four-membered ring product **6d** was produced via a metal facilitated ring contraction of urea derivative **6c**.

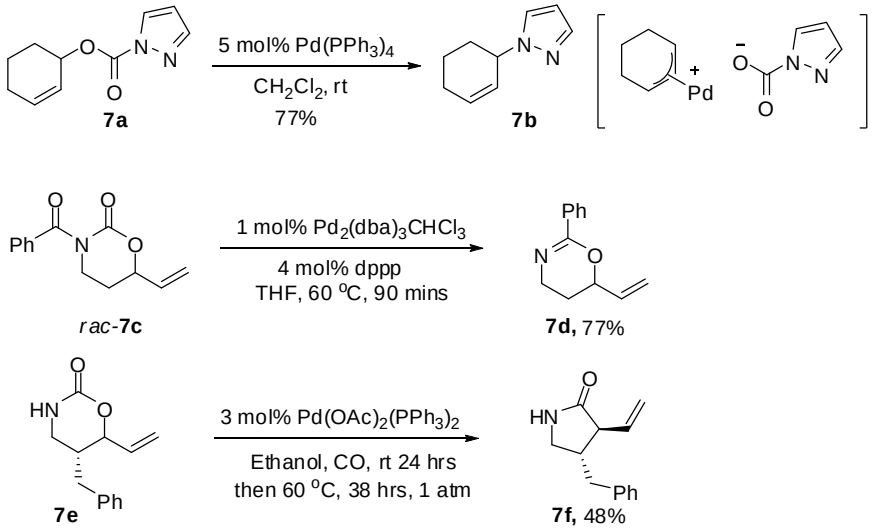
Scheme 4 *Ring synthesis via six-membered ring contractions*



2.3 Pd-Catalyzed Azetidine Synthesis via Decarboxylative Ring Contraction

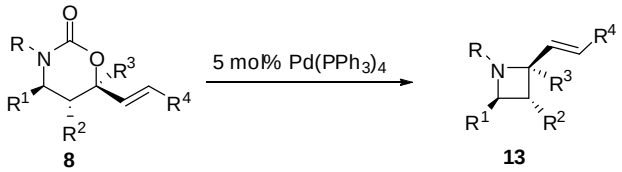
Our group has shown that cyclohexenyl pyrazoyl carboxylate **7a** undergoes a similar decarboxylative amination to furnish product **7b** in good yield as shown in Scheme 5.[32] It is also known that 6-vinyl-1,3-oxazinanones undergo ring opening and decarboxylation in the presence of palladium catalysts, and the intermediate palladium allyl complexes have been trapped by pendant nucleophiles and CO to yield oxazine **7d** and pyrrolidinone **7f** respectively.[33, 34]

Scheme 5 *Nitrogen nucleophiles in Pd-catalyzed allylation reactions*



On the basis of this precedent, we hypothesized that vinyl oxazinanones **8** would undergo decarboxylative ring contractions and allow facile generation of vinyl azetidines **13** (Scheme 6).

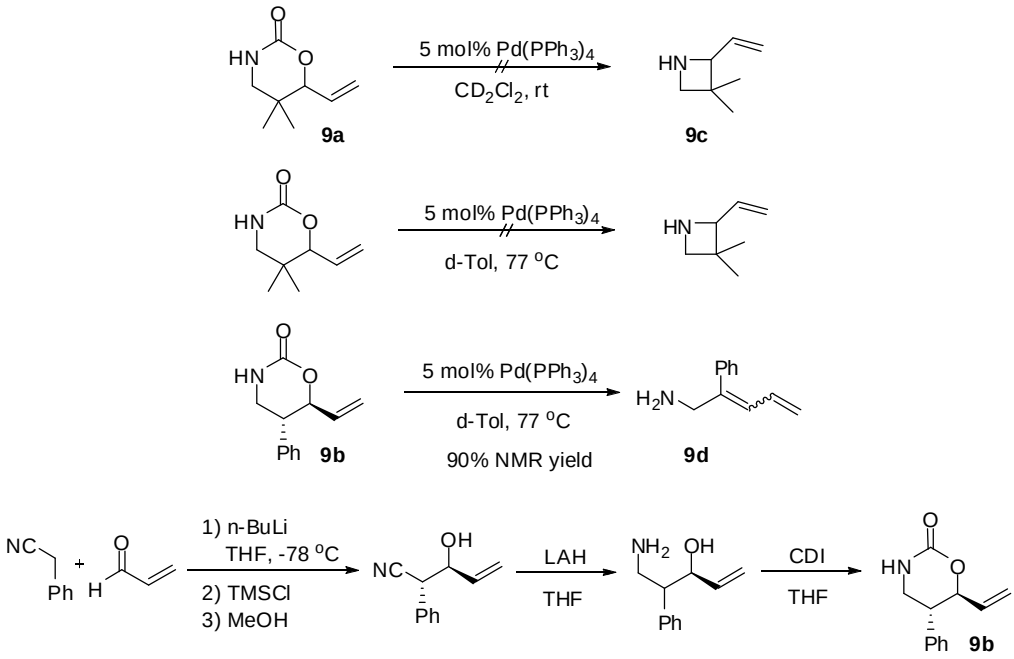
Scheme 6 *Decarboxylative ring contraction*



To begin, free allylic carbamates **9a** and **9b** were allowed to react under our standard conditions as shown in Scheme 7. However, substrate **9a** did not react even at 77 °C in toluene. This is possibly due to the steric hinderance of geminal dimethyl substituents or the difficulty of generating an unstabilized amide nucleophile by decarboxylation. That decarboxylation can take place under these conditions is

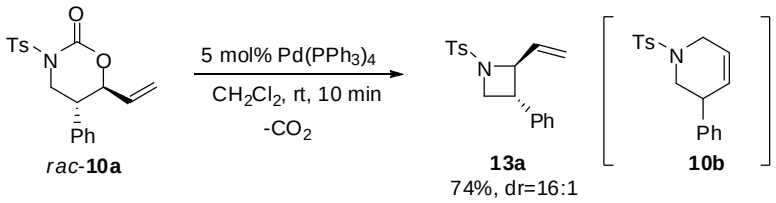
shown by the formation of butadiene product **9d** from exclusive β-hydride elimination from vinyl oxazinanone **9b**. This suggested that the amide anion generated was too basic, which promoted elimination. Also showed here is a scheme for preparing the vinyl oxazinanone **9b**.

Scheme 7 *Decarboxylative ring contractions with N-unprotected carbamates*



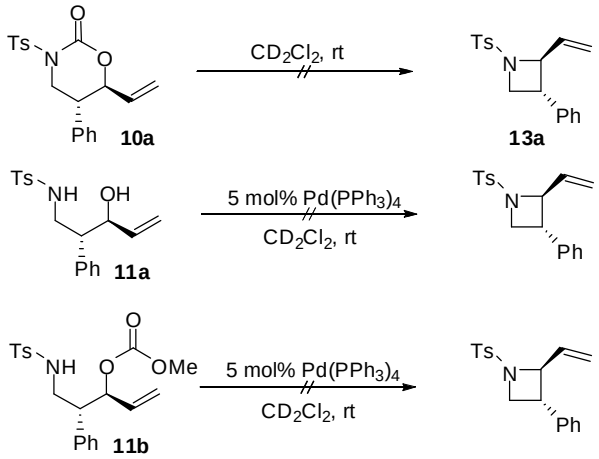
With the goal of reducing the basicity of nitrogen, we turned to the reaction of tosyl-protected carbamates. Thus, **10a** was prepared from the corresponding 1,3-amino alcohol by treatment with carbonyl diimidazole.[33, 35] Indeed, allowing *trans*-**10a** (>19:1 dr) to react in the presence of 5 mol% of $Pd(PPh_3)_4$ in CH_2Cl_2 at 25 ^oC led to rapid evolution of CO_2 and formation of the vinyl azetidine **13a** in 74% yield with no observable formation of the tetrahydropyridine **10b** (Scheme 8).[36, 37]

Scheme 8 *Diastereoselective decarboxylative azetidine synthesis*



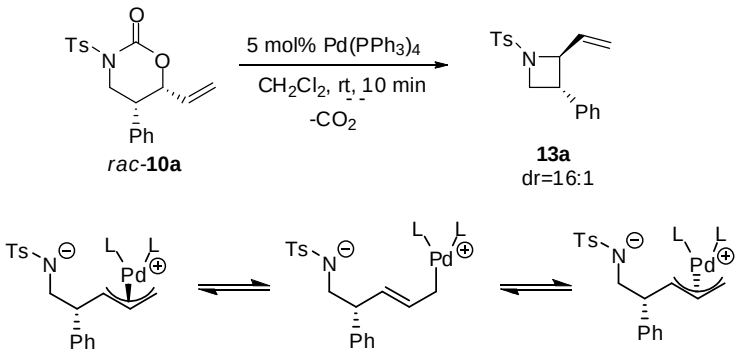
Next, several control experiments were conducted to probe the effect of the palladium catalyst (Scheme 9). No reaction occurred without catalyst and starting material **10a** was recovered. Similarly, amino alcohol **11a** was treated with our standard reaction conditions, in which azetidiene product **13a** was not formed and reactant **11a** remained intact. Lastly, treatment of compound **11b** with 5 mol% of $Pd(PPh_3)_4$ afforded a messy polymeric mixture, which further demonstrated that 6-vinyl-1,3-oxazinanones are the best substrates for diastereoselective, decarboxylative ring contractions.

Scheme 9 *Control experiments*



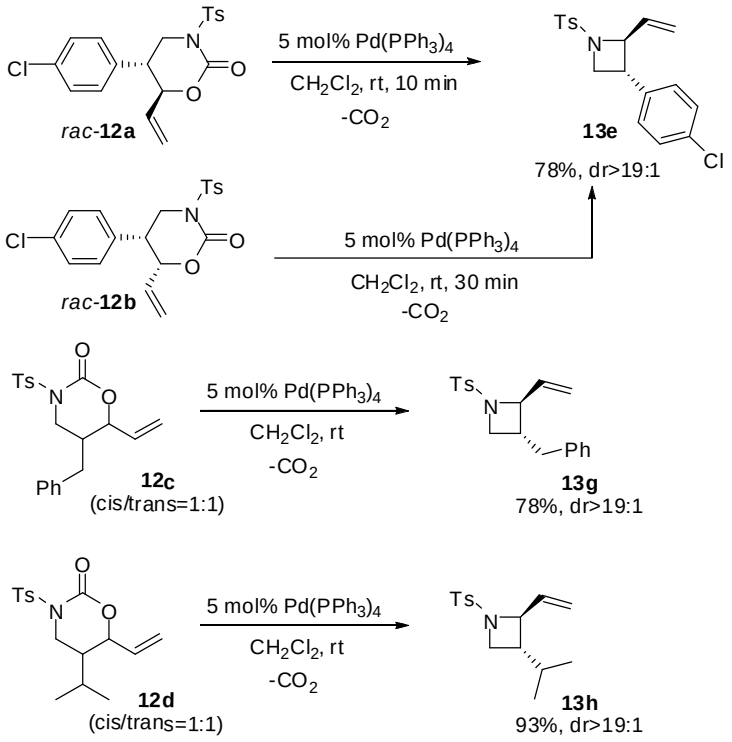
Turning back to the successful ring contraction, we noted that the ratio of diastereomers in the product azetidine (16:1) was slightly smaller than that of the starting material (>19:1). This suggested that the diastereomers were interconverting on the time scale of the cyclization. To test this hypothesis, *cis*-**10a** was prepared and subjected to the same reaction conditions (Scheme 10). Although the rate of the reaction with *cis*-**10b** was somewhat slower than that with *trans*-**10a**, the product was identical. Thus, epimerization through π-σ-π allyl interconversion is faster than cyclization (Scheme 10).[38] This is an important observation because it allows the synthesis of highly diastereoenriched azetidines from diastereomixtures of the cyclic allylic carbamates.

Scheme 10 *Diastereoselective decarboxylative azetidine synthesis*



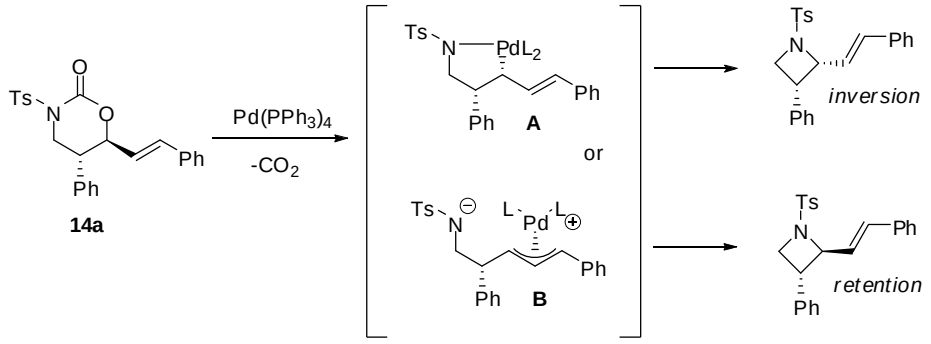
As further proof, two diastereoisomers **12a** and **12b** produced identical vinyl azetidine product **13e** in 78% yield (Scheme 11). More importantly, highly diastereoenriched azetidines **13g** and **13h** were synthesized from 1:1 diastereomixtures of the cyclic allylic carbamates **12c** and **12d**.

Scheme 11 *Diastereoenriched azetidine syntheses*



Rapid formation of the vinyl azetidine can be explained by one of two possible mechanisms (Scheme 12). First, nitrogen may coordinate to palladium to form a five-membered metallacycle **A** that would give rise to the azetidine upon reductive elimination.[39, 40] Second, a free nitrogen anion might preferentially undergo backside attack at the 4-carbon of π-allyl complex **B**. The two mechanisms are readily distinguished by the stereochemistry of the cyclization. Reductive elimination from a five-membered metallacycle should give overall inversion of stereochemistry, and backside attack by an amide anion should result in overall retention of stereochemistry.[41]

Scheme 12 *Two possible mechanisms of the vinyl azetidines formation*

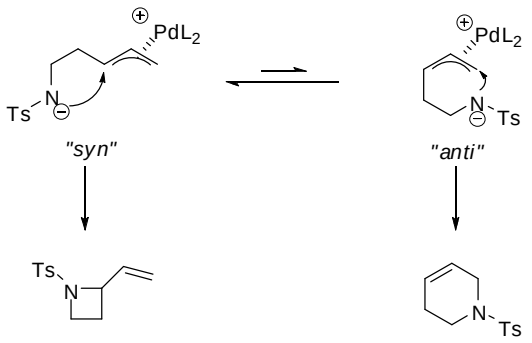


The stereochemical analysis of the ring contraction can only be performed if the substrate does not epimerize. Therefore, substrate **14a** was chosen for study because the initial stereochemistry of the allyl alcohol cannot be lost by a π-σ-π epimerization mechanism that is common for terminally unsubstituted π-allyl complexes. The azetidine formed from **14a** under our standard reaction conditions was shown to be the *trans* isomer by nOe experiments, indicating that the reaction proceeds with overall retention of stereochemistry. Thus, the reaction likely proceeds by backside attack of the amide anion on the π-allyl ligand via **B**.

Regarding the preferential four-member cyclization, Rutjes and Hiemstra have suggested a stereoelectronic origin for the regioselectivity of related cyclizations of β-aminoallenes.[36] Monosubstituted palladium π-allyl complexes can adopt two conformations, and the *syn* conformation is thermodynamically favored because it avoids A1,3-strain (Scheme 13). Although the *syn* conformation can readily give rise

to the vinyl azetidine, the *anti* conformation is required for formation of the tetrahydropyridine derivative.

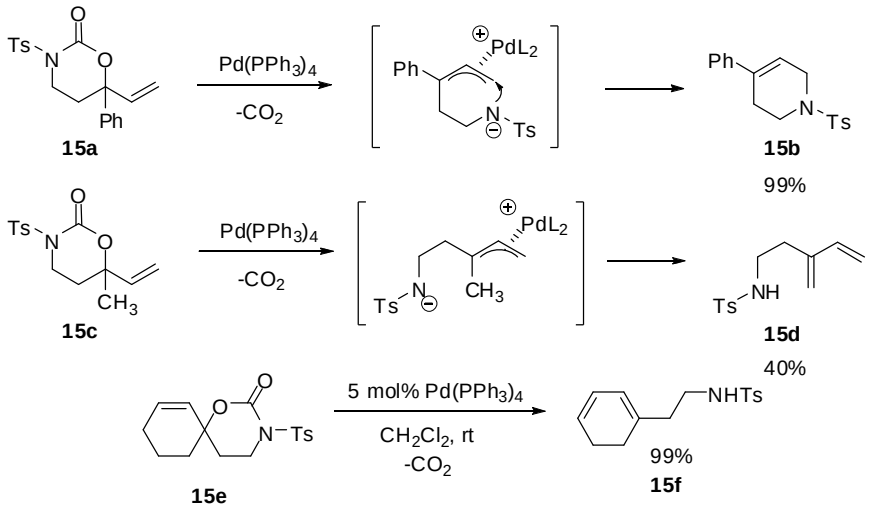
Scheme 13 *Stereoelectronic origin for the preferential four-membered cyclization*



To probe this mechanistic hypothesis, a 6-phenyl vinyloxazinanone **15a** was prepared. Such a substrate should prefer to place the sterically smaller amino alkyl fragment in the *anti* position and would be expected to preferentially form the tetrahydropyridine isomer (Scheme 14) if the Rutjes mechanism is correct. Indeed, treatment of **15a** under standard reaction conditions produced tetrahydropyridine **15b** in quantitative yield. Furthermore, scrutiny of the reaction progression by ^{1}H NMR spectroscopy showed no evidence for intermediate azetidine formation, indicating that tetrahydropyridine **15b** is the kinetic product. A similar 6-methyl-substituted derivative **15c** was prepared and allowed to react with 5 mol% of $Pd(PPh_3)_4$ in CH_2Cl_2. In this case, deprotonation is favored, and diene **15d** is the only observable product of the reaction. Bicyclic vinyl oxazinanone **15e** was also tested, in which

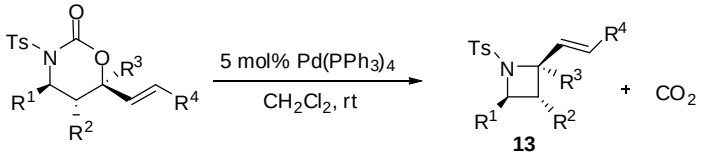
deprotonation occurred exclusively to produce diene product **15f** in a quantitative yield.

Scheme 14 *Stereoelectronic effects on the ring cyclizations*



Although the above considerations eliminate the possibility of formation of tertiary C-N bonds *via* decarboxylative ring contraction, other substitution patterns are allowed. For example, both 5-alkyl- and 5-aryl-substituted 1,3-oxazinanones provide good yields and selectivities for *trans*-1,2-vinyl azetidines (Table 1). The 4-substituted vinyl oxazinanones react similarly, but they provide the *syn*-1,3-vinyl azetidines with good diastereoselectivity. The stereochemical outcome for either case can be rationalized on the basis of the preference for substituents to occupy the pseudoequatorial positions of the four-membered transition state **16a** for cyclization as shown in Scheme 15.

Table 1 *Yields and diastereoselectivities for decarboxylative ring contractions*

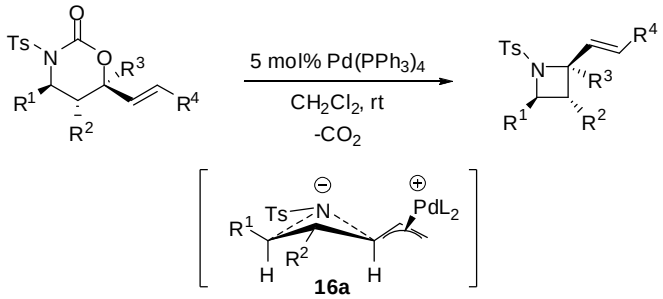


13

R_1	R_2	R_3	R_4	Product	Yield (dr)[a]
H	Ph	H	H	**13a**	74 (16:1)
H	Ph	H	Ph	**13b**	62 (>19:1)
H	H	Ph	H	**13c**	<1
H	H	Me	H	**13d**	<5
H	*p*-ClC_6H_4	H	H	**13e**	78 (>19:1)
H	*p*-$MeOC_6H_4$	H	H	**13f**	84 (14:1)
H	CH_2Ph	H	H	**13g**	60 (8.5:1)[b]
H	$CH(CH_3)_2$	H	H	**13h**	93 (>19:1)[b]
Ph	H	H	H	**13i**	92 (>19:1)
Me	H	H	H	**13j**	78 (8:1)

[a] Yield and dr of isolated product *via* column chromatography. [b] Prepared from ca. 1:1 *syn*/*anti*-**1**.

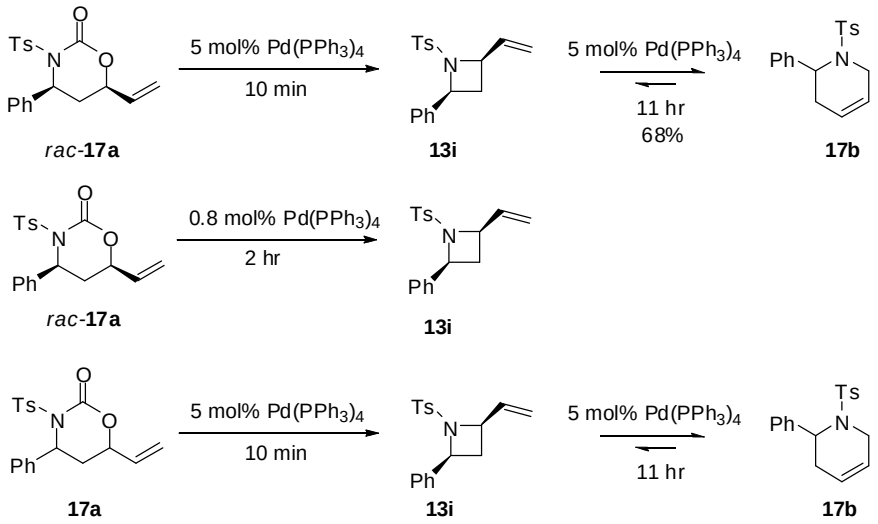
Scheme 15 *Transition state for the decarboxylative ring contraction*



16a

On the basis of literature reports, the formation of vinyl azetidines is expected to be reversible.[36, 42-45] In accord, treatment of **17a** for 10 min at room temperature provided the vinyl azetidine **13i**; however, prolonged standing in the presence of the Pd(0) catalyst resulted in complete conversion to the thermodynamically more stable tetrahydropyridine isomer **17b** (Scheme 16). A diatereomixture **17a** was treated with the standard reaction conditions. As expected, diastereoenriched azetidine product **13i** was formed at comparable rates. Also to be noted here is that lower catalyst loading (0.8 mol% of $Pd(PPh_3)_4$) completely shut the isomerization off and the thermodynamic tetrahydropyridine isomer **17b** was not formed even after three days. Thus, the rapid reaction rate and mild conditions of azetidine formation are important because they allow one to avoid isomerization which can be significant at elevated temperatures and/or catalyst loadings.[36]

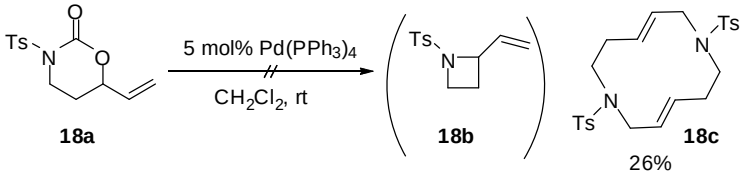
Scheme 16 *Isomerization of azetidines to thermodynamically stable pyridines*



2.3.1 Other observations

Unsubstituted vinyl oxazinanone **18a** was prepared and treated with 5 mol% of $Pd(PPh_3)_4$ in CH_2Cl_2 (Scheme 17). In this case a (presumably) polymeric mixture was formed within 10 minutes at room temperature, even though a small amount of twelve-membered dimer **18c** was separated *via* column chromatography (26% yield). This product was confirmed by two triplet double ^1H signal (1:1 ratio) at 5.4 and 5.6 ppm respectively in the ^1H NMR spectrum.

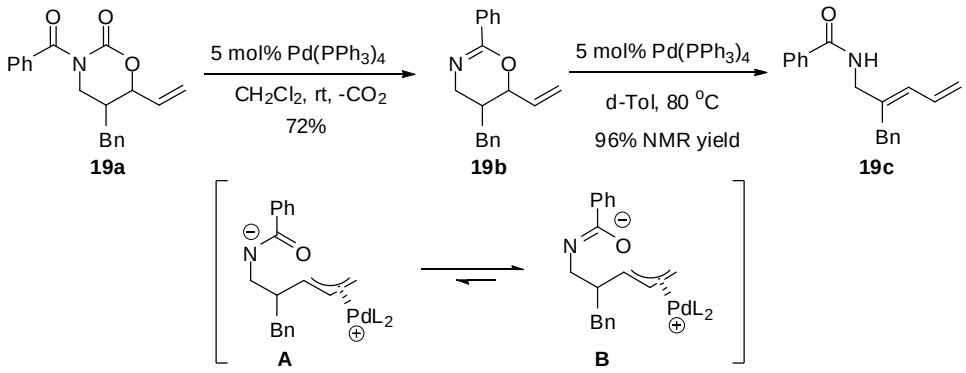
Scheme 17 *Investigation on reaction scope*



Benzoyl-protected substrate **19a** was prepared and allowed to react with $Pd(PPh_3)_4$ in CH_2Cl_2 at room temperature (Scheme 18). Instead of the four-membered azetidine product, a six-membered oxazine **19b** was produced as a 1.7:1 diastereomixture in 72% yield. Presumably, a zwitterionic intermediate **A** was generated upon decarboxylation, which was in resonance with intermediate **B**. This intermediate is perfectly set up for the oxazine ring closure which is consistent with the related reaction discovered by Cook.[34] We were also curious whether the oxazine product isomerizes at higher temperature. In that regard, compound **19b** was treated

with 5 mol % of $Pd(PPh_3)_4$ in toluene at 80 ^oC and a diene product **19c** was formed cleanly in 96% NMR yield.

Scheme 18 *Substrate with a different N-protection group*



In summary, we have developed a unique ring contraction of cyclic carbamates that diastereoselectively produces vinyl azetidines. Importantly, the reaction proceeds under mild conditions and produces CO_2 as the only byproduct.

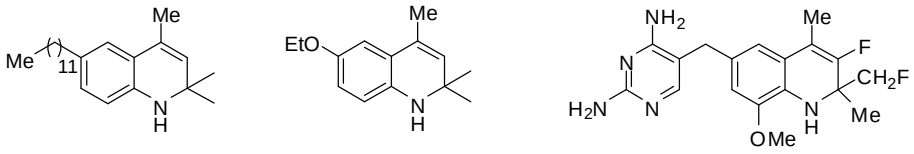
2.4 The Importance of Bioactive Quinolines and Their Derivatives

Other well-known *N*-heterocycles are quinolines and their derivatives such as 1,2-dihydroquinoline, isoquinoline and tetrahydroquinoline. These compounds occur widely in nature and find many applications including their use as building blocks for organic synthesis, and as potential candidates for pharmaceuticals, antioxidants, agrochemicals and dyes.

The 1,2-dihydroquinoline alkaloids are an interesting type of compounds, which

can be converted to quinolines by oxidation and in that regard, two dihydroquinoline derivatives **20a** and **20b** have been used in rubber production as antioxidants (Figure 5).[46] Substituted 1,2-dihydroquinoline derivative **20c** has shown potent antibacterial activity and high inhibition of *Escherichia coli* dihydrofolate reductase.[47] In other cases, reduction[48] or electrophilic addition[49, 50] to the double bond of 1,2-dihydroquinoline generates 1,2,3,4-tetrahydroquinoline derivatives.

Figure 5 *1,2-Dihydroquinoline alkaloids*

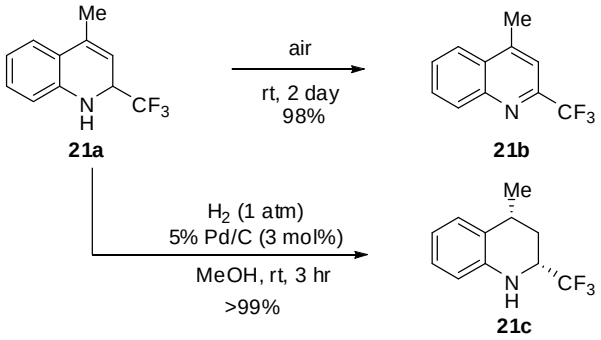


20a **20b** **20c**

2.5 Overview of 1,2-Dihydroquinoline Synthesis

Even though 1,2-dihydroquinolines have not drawn a lot of attention, possibly due to their inherent instability and the scarcity of natural products bearing a 1,2-dihydroquinoline structure element, they are a potential building block for quinoline and tetrahydroquinolin alkaloids.[51] For example, Taguchi recently reported a convenient synthesis of fluorinated 1,2-dihydroquinolines synthesis from substituted anilines (Scheme 19).[52] Dihydroquinoline **21a** was smoothly converted to quinoline **21b** or tetrahydroquinoline **21c** by either air oxidation or reduction respectively.

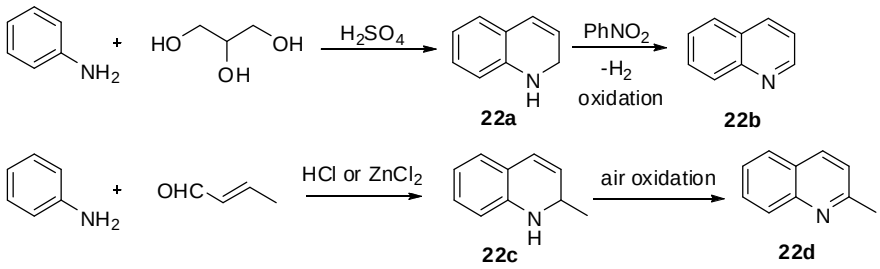
Scheme 19 *Modification of 1,2-dihydroquinoline derivatives*



2.5.1 Skraup and Skraup/Doebner-Miller procedures starting with aniline derivatives

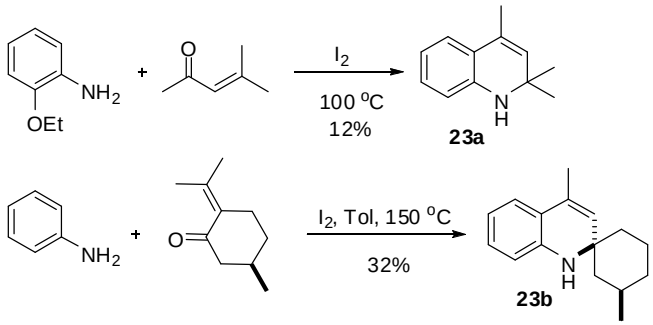
Quinoline derivative synthesis has drawn a lot of attention due to their biological activities (Chapter 2.4). Traditionally, quinolines were synthesized from the corresponding aniline derivatives *via* the Skraup procedure shown in Scheme 20.[53] Glycerol was used as the synthetic equivalent of acrolien, which cyclized with aniline to generate a 1,2-dihydroquinoline intermediate **22a**, followed by oxidation to give quinoline product **22b**. The related Skraup/Doebner-Miller procedure involves a reaction of aniline with *α,β*-unsaturated aldehydes or ketones in the presence of HCl or Lewis acids. Air oxidation of intermediate **22c** produced the quinoline product **22d**. However, those transformations require a large amount of sulfuric acid or strong Lewis acid combined with harsh reaction conditions. Thus, the products were generally obtained in low to moderate yields.

Scheme 20 *Skraup and Skraup/Doebner-Miller Procedures*



A modified Skraup/Doebner-Miller procedure has been adopted for 1,2-dihydroquinoline synthesis, in which disubstituted mesityl oxide derivatives were employed instead (Scheme 21).[23,24] Compounds **23a** and **23b** were synthesized by treatment of anilines with mesityl oxide derivatives catalyzed by iodine. As such, the aromatization of the 1,2-dihydroquinolines would require losing one molecule of methane (Riehm quinoline synthesis), which is more difficult than losing a molecule of hydrogen.

Scheme 21 *Modified Skraup/Doebner-Miller type reactions*



The major drawback of this procedure is the low yield of dihydroquinoline product due to the competing polymerization. Recently solvent-free Skraup Doebner-

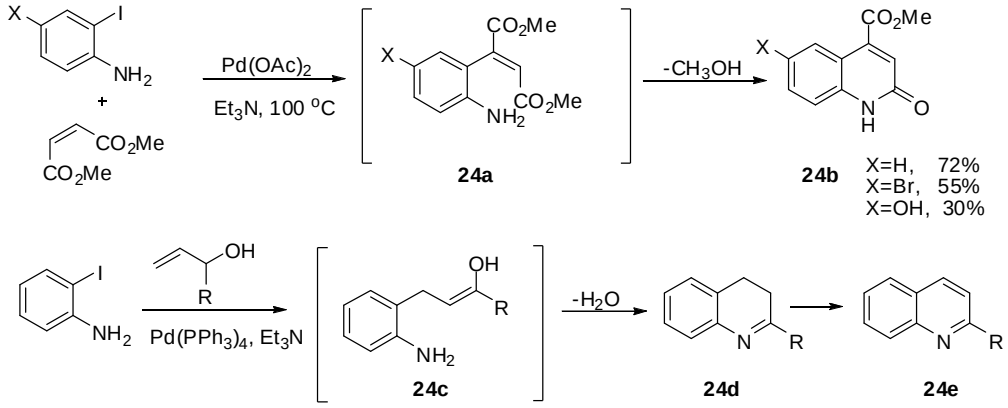
Miller reactions have been developed with microwave radiation.[54] For example, a series of dihydroquioline products were synthesized in moderate yields by treatment of aniline with enones in the presence of silica gel charged with indium trichloride under microwave conditions.

2.5.2 Transition-metal catalyzed 1,2-dihydroquinoline synthesis

There are several drawbacks of traditional methods for 1,2-dihydroquinoline or quinoline synthesis. For example most reactions need high temperature in the presence of a strong Bronsted or Lewis acids. Functional group compatibility, decomposition of products, and competing side reactions are always the concerns under those harsh conditions. To potentially alleviate these problems, transition metal catalysts have been introduced into this scenario.

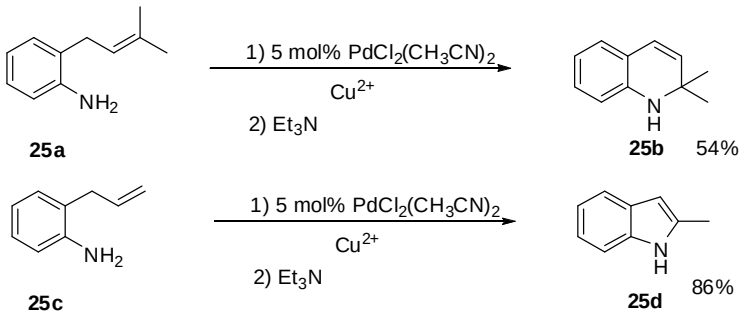
Transition metal-catalyzed heteroannulation reactions have been extensively studied due to the potential biological and pharmaceutical activity of those heterocyclic compounds. For example, substituted 2-iodoanilines have been shown to undergo a Heck reaction with *cis*-dimethyl maleate to generate *trans*-olefin intermediate **24a**, which upon cyclization produced quinolone **24b** in moderate yields (Scheme 22). Larock reported a similar procedure with allylic alcohols, in which *β*-hydride eliminations afforded enol intermediates **24c**, followed by intramolecular condensations and oxidations to furnish quinolines **24e**.[55]

Scheme 22 *Heck- type coupling reaction*



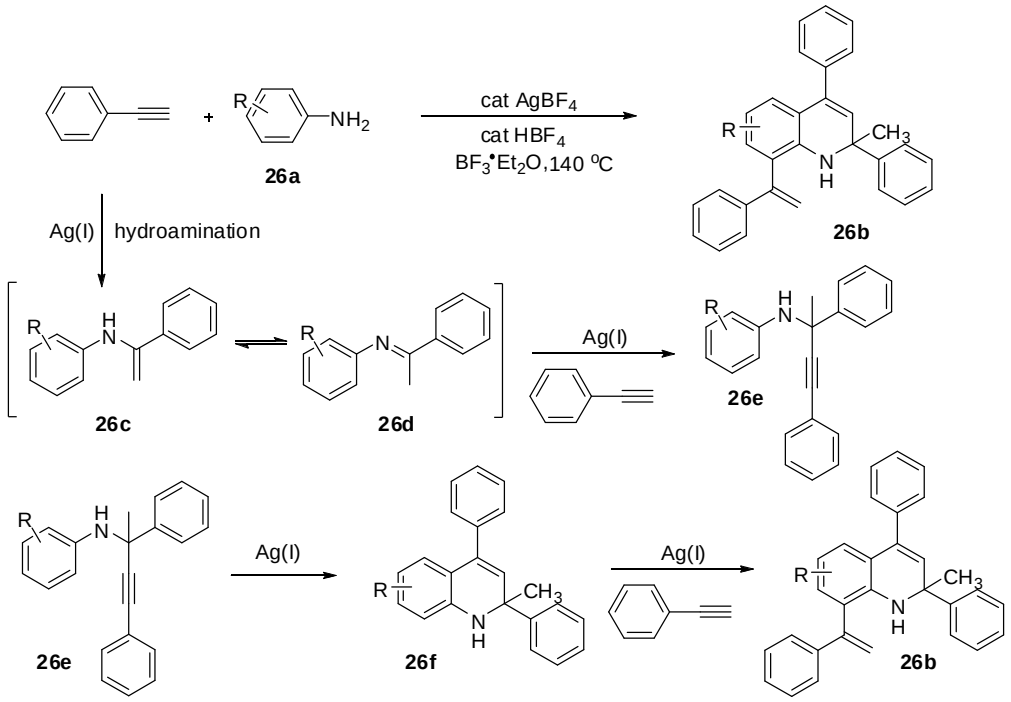
Another procedure involves intramolecular amination of substituted 2-allylanilines **25a** and **25c** produced dihydroqinoline **25b** and indole **25d** respectively in the presence of catalytic amount of $PdCl_2(CH_3CN)_2$ (Scheme 23). Interestingly, different chemoselectivity displayed with simple allyl side chain in which a 5-exo-trig was favored over 6-endo-trig, whereas the dimethyl substituted allylaniline **25a** predominantly generated the 6-endo-trig product. The reason possibly resides in the stability of a tertiary carbocation.

Scheme 23 *Intramolecular amination of olefines*



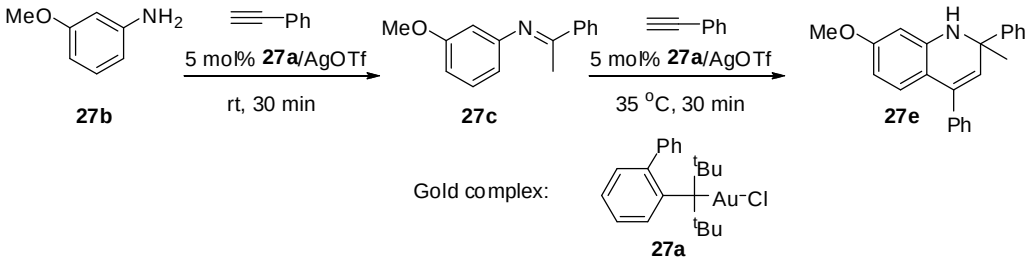
Gold and silver have been used for the functionalization of alkynes based on their unique Lewis acidity. In 2005, Li reported their results on hydroamination of alkynes with a silver catalyst toward the synthesis of highly substituted 1,2-dihydroquinolines.[56] A possible mechanism was also postulated as shown in Scheme 24. Silver-catalyzed hydroamination generates an enamine intermediate **26c** in tautomerization with ketimine **26d**, and reaction of ketimine with another molecule of alkynes yields propargylamine **26e**, followed by intramolecular cyclization and further addition to give highly functionalized 1,2-dihydroquinoline product **26b**.

Scheme 24 *Silver-catalyzed 1,2-dihydroquinoline synthesis*



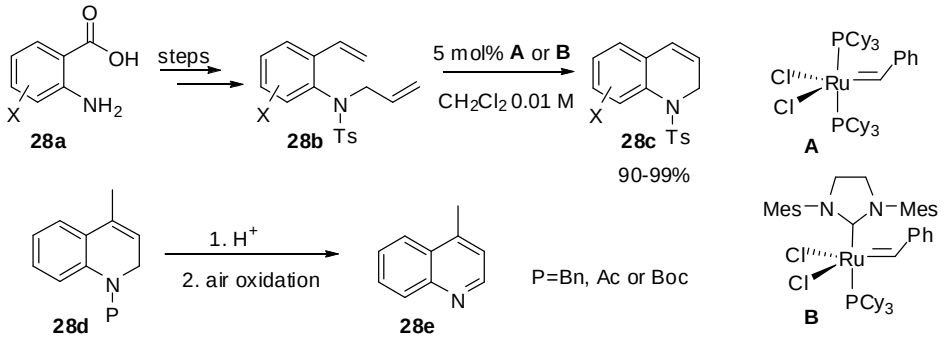
Gold complexes were also found to catalyze similar transformations. Recently, an efficient synthesis of quinolines and dihydroquinolines catalyzed by Au(I) was disclosed by Che under microwave radiation (Scheme 25).[57] Product **27e** was prepared by a Au-catalyzed tandem hydroamination-hydroarylation of phenyl acetylene in 91% yield.

Scheme 25 *Gold-catalyzed 1,2-dihydroquinoline synthesis*



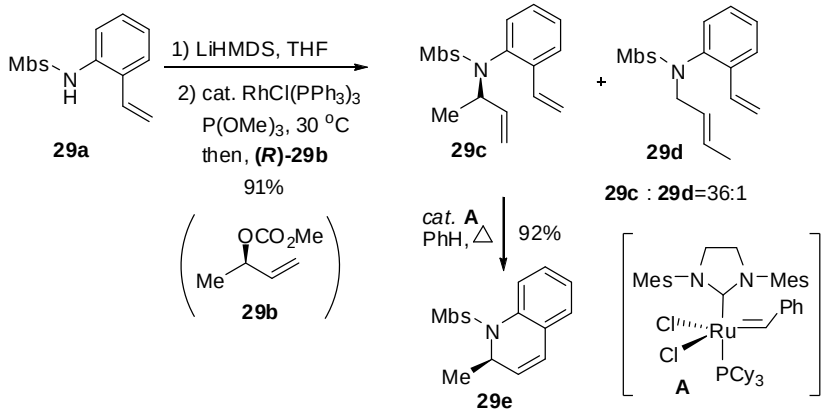
Finally, ring-closing metathesis strategies have also been employed in 1,2-dihydroquionline synthesis (Scheme 26). For example, 2-vinyl allylamines **28b** underwent ring-closing metathesis smoothly in the presence of Grubbs' catalyst **A** or **B** to generate the dihydroquinoline product **28c** in high yield.[58] Dihydroquinolines with acidic sensitive *N*–protecting groups **28d** were subsequently deprotected and air-oxidized to give quinoline product **28e** during silica gel chromatography in good to excellent yield.

Scheme 26 *RCM (Ring-closing metathesis) for 1,2-dihydroquinoline synthesis*



Evans reported an efficient synthesis of 1,2-dihydroquionline rings using a regioselective allylic amination combined with ring-closing metathesis in the presence of rhodium catalysts as shown in Scheme 27. Vinyl aniline **29a** reacted with enatiopure allylic carbonate **29b** to produce the RCM reaction precursor **29c** in excellent reigoselctivity (36:1). Upon treatment with Grubbs's catalyst **A**, 1,2-dihydroquionline product **29e** was furnished in 92% yield.

Scheme 27 *Allylic amination combined with RCM for 1,2-dihydroquinoline synthesis*

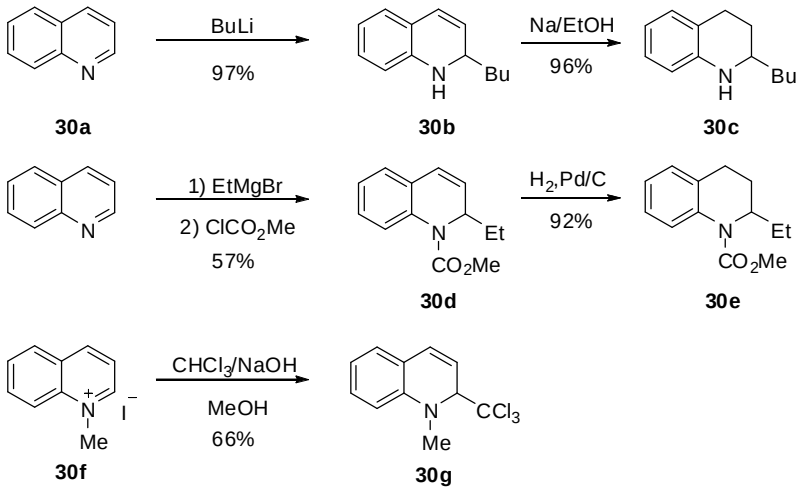


Other transition metals such as copper,[59, 60] manganese[61] and iron[62] etc have also shown catalytic activity toward the synthesis of dihydroquinolines. However, due to their similarity with the transition metals mentioned above, those catalysts are not covered in this dissertation.

2.5.3 1,2-dihydroquinolines synthesis via modification of quinoline rings

It has been shown that nucleophilic addition to quinoline derivatives furnishes 1,2-dihydroquinoline products, which were then transformed to tetrahydroquinolines through reduction (Scheme 28). For example, treatment of quinoline **30a** with n-butyl lithium or ethyl magnesium bromide produces 1,2-dihydroquinolines **30b** and **30d** in 97% and 57% yield respectively.[48, 63, 64] Interestingly, activation of quinoline **30a** by converting it to iminium salt **30f** allowed the nucleophilic attack of weaker nucleophiles, and in fact compound **30g** was obtained in 66% yield.[65]

Scheme 28 *Conversion of quinolines to 1,2-dihydroquinolines*

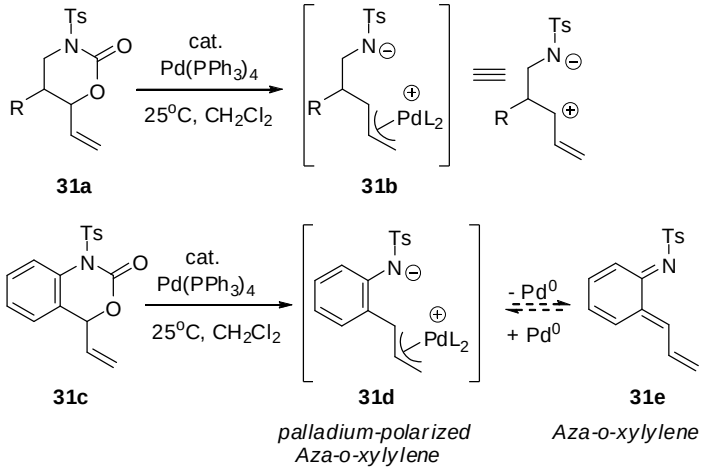


2.6 Decarboxylative Dihydroquinoline Synthesis *via* Aza-ortho-xylylene Intermediates

Even though there are many reported procedures for 1,2-dihydroquinoline synthesis, the current methods still have some limitations in regard to the cost and availability of substrates, prolonged reaction times at high temperature, strongly acidic conditions and functional group compatibility. As such, a mild and efficient method for dihydroquinoline syntheis is still highly desirable.

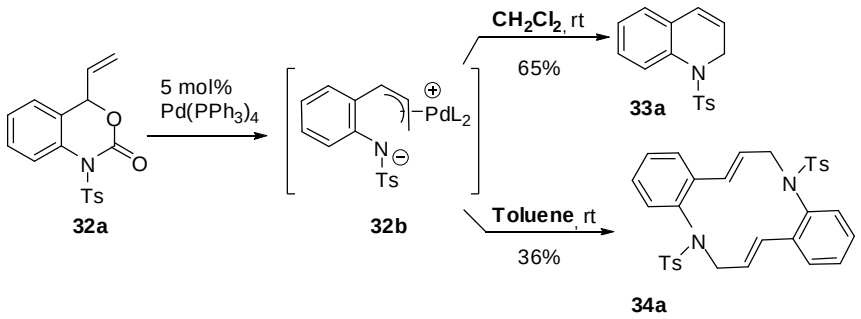
We have previously reported that vinyl oxazinanones **31a** underwent catalytic diastereoselective decarboxylative ring contraction to form vinyl azetidines under mild conditions in good yield.[66] A zwitterionic π-allyl palladium complex **31b** was proposed as the intermediate (Scheme 29). We reasoned that conjugation of the two charges would allow mild catalytic generation of aza-*ortho*-xylene intermediates.[67] Such a scenario creates two possibilities. The zwitterionic intermediate can potentially expel Pd(0) to produce a free aza-*o*-xylylene **31e**. Alternatively, if Pd remains coordinated, then a polarized aza-*o*-xylylene intermediate **31d** will result.[68] Then substituted 1,2-dihydroquinolines could be formed via either a cyclization of the π-allyl intermediate **31d** or a electrocyclization of the free aza-*o*-xylenene **31e**.[69]

Scheme 29 *Zwitterionic π-allyl palladium intermediates*



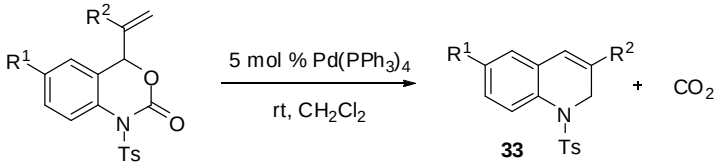
To begin, the parent vinyl benzoxazinanone **32a** was prepared and subjected to $Pd(PPh_3)_4$ in CH_2Cl_2 at room temperature. In contrast to the saturated analogs which undergo ring contraction to azetidines, **32a** produced the hydroquinoline **33a** in 65% yield (Scheme 30). Interestingly, conducting the same reaction in toluene solvent produces the 12-membered dimer **34a** exclusively. Even though the dimer product **34a** was obtained in 36% isolated yield, this compound was formed cleanly as shown by ^{1}H NMR spectroscopy. Since it is improbable that such a dimer could arise from concerted [6+6] cycloaddition, it seems likely that Pd-polarized aza-*o*-xylylene **32b** is the intermediate in these reactions.

Scheme 30 *Solvent effects on the chemoselectivity*



Next we turned our attention to investigating the reaction scope. It since has been shown that various vinyl benzoxazinanones undergo smooth intramolecular decarboxylative allylic aminations and the dihydroquinoline products were obtained in good to excellent yield (Table 2).

Table 2 *Yields of dihydroquinolines via intramolecular decarboxylative allylations*

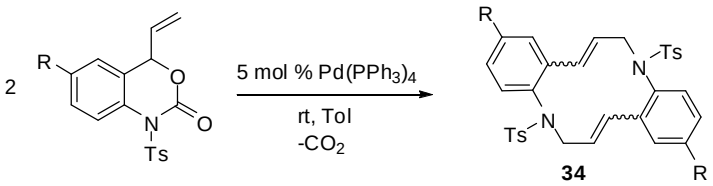


R^1	R^2	Product	Yield% [a]
H	H	**33a**	65[b]
H	Me	**33b**	77
p-Me	H	**33c**	50[b]
p-Me	Me	**33d**	94
p-F	H	**33e**	51[b]
p-F	Me	**33f**	82
p-MeO	H	**33g**	80[b]
p-MeO	Me	**32h**	92

[a] Yield of isolated product *via* column chromatography. [b] The by-products were dimers or polymers, which were somehow suppressed by performing the reaction in dilute solution with lower catalyst loading.

The clean formation of dimer products was also interesting to us and treatment of different vinyl benzoxazinanones with a catalytic amount of $Pd(PPh_3)_4$ in toluene gave the 12-membered ring products **34** in good to excellent yield at room temperature as shown in Table 3. The coupling constants of olefins suggested a *trans*-geometry in compounds **34a**, **34b** and **34c** (J = 16.2 Hz); while compound **34d** (J = 9.8 Hz) was formed with a *cis*-olefin geometry. At this point, we don't have a reasonable explanation for this stereoselectivity.

Table 3. *Yields of dimer products via intermolecular decarboxylative cycloaddition*



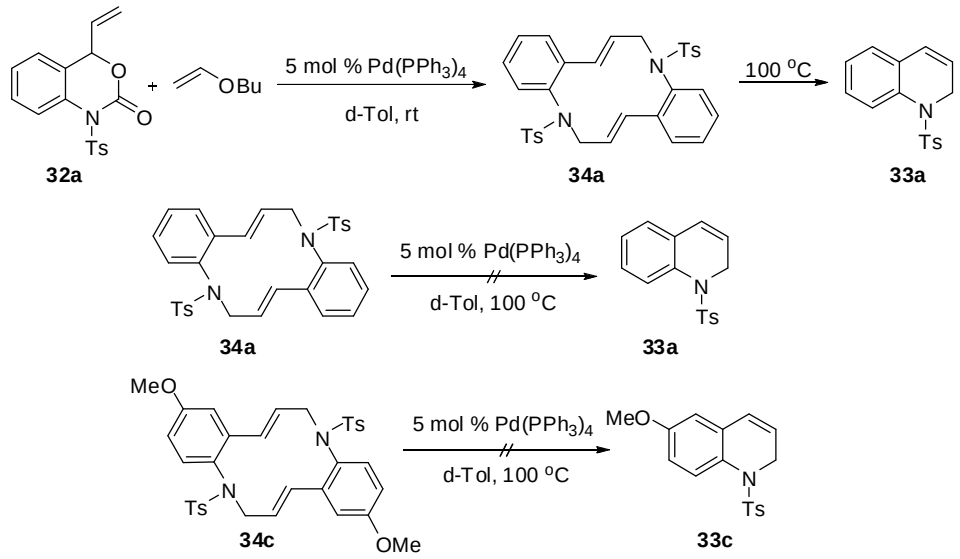
R	Product	Yield%
H	**34a** [a]	36 [c]
Me	**34b** [a]	87
OMe	**34c** [a]	94
F	**34d** [b]	92 [d]

[a] Dimer products with a *trans*-olefin geometry. [b] Dimer product with a *cis*-olefin geometry. [c] Yield of isolated product *via* column chromatography and **34a** was formed cleanly as shown by ^{1}HNMR spectroscopy. [d] This reaction was carried out in dichloroethane at 60 ^{o}C.

To further shed light on the reaction mechanism, vinyl benzoxazinanone **32a** was allowed to react with vinyl butyl ether in the presence of 5 mol% $Pd(PPh_3)_4$ in toluene as shown in Scheme 31. If a free aza-*o*-xylylene is indeed being formed, then one would predict that it would undergo [4+2] cycloaddition with vinyl butyl ether.[70]

However, the dimer product **34a** was formed smoothly in the presence of a dienophile and no [4+2] cycloaddition reaction occurred. Interestingly, if the reaction was heated to 100 ^{o}C, dimer product **34a** cleanly isomerized to the thermodynamically more stable dihydroquinoline product **33a**. This reaction was also performed in dichloromethane, in which dihydroquinoline **33a** was formed along with the dimer **34a** in a ratio of 4:1. These observations suggest that palladium catalyzes the equilibration of dimers **34** and dihydroquinolines **33**. To test this hypothesis, isolated dimer products **34a** and **34c** were treated with catalytic amount of $Pd(PPh_3)_4$ in toluene at 100 ^{o}C; however no equilibration occurred and the reactant kept intact over the course of the reaction. One thing to note here is that palladium black precipitated out the reaction solution at high temperatures.

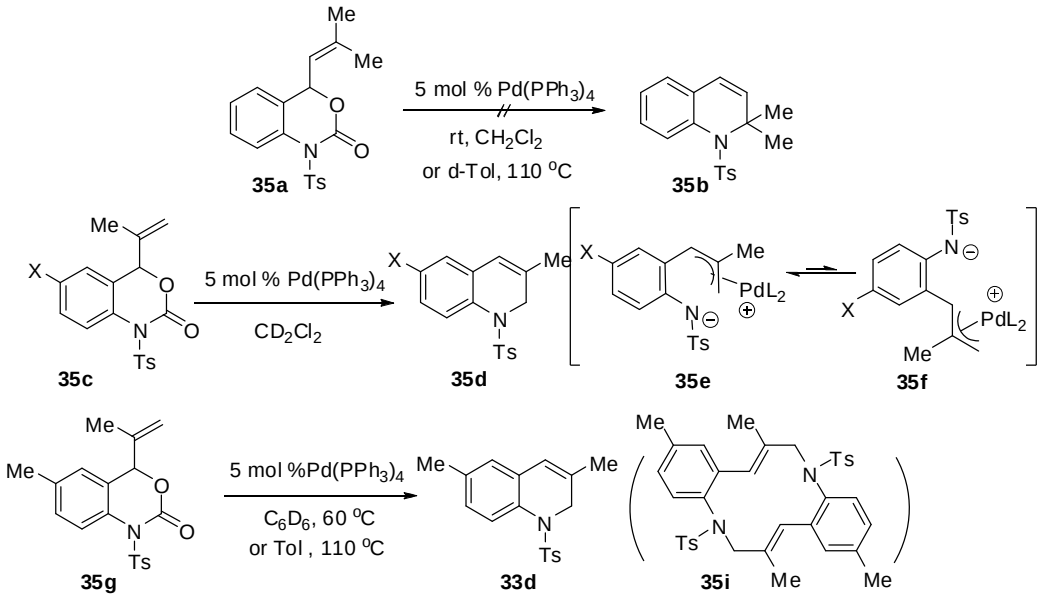
Scheme 31 *Kinetic vs thermodynamic product*



General observations related to dihydroquinoline synthesis

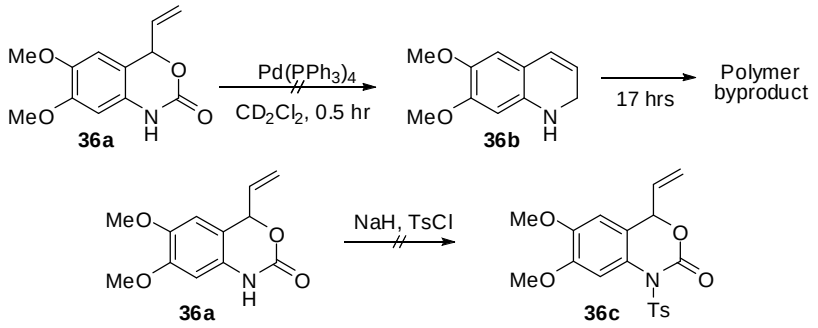
Vinyl benzoxazinanone **35a,** with a terminal disubstituted olefin, was prepared and treated with our standard reaction conditions. No reaction occurred and starting material was recovered either at room temperature or 110 ^{o}C, which suggests that the coordination between olefin and catalyst must occur first for the reaction to proceed (Scheme 32). Also of note is that dihydroquinolines **35d** were produced in high yield with no observation of dimer formation. Actually when we tried to synthesize dimer **35i,** the intramolecular cyclization was much faster and dihydroquinoline **33d** was generated exclusively.

Scheme 32 *Intramolecular vs intermolecular cyclization*



An interesting observation was found with substrate **36a** with two electron donating groups on the phenyl ring as illustrated in Scheme 33. Treatment of **36a** with 5 mol% $Pd(PPh_3)_4$ in methylene chloride did not generate the dihydroquinoline product **36b**, even though decarboxylation did occur and a new product was formed, whose structure is yet to be determined. However this compound was not stable under the reaction conditions and polymeric products were formed if the reaction mixture was allowed to stand overnight. Similarly, the Ts-protection of carbamate **36a** was problematic due to the generation of a polymer-like mixture. This result seems to indicate that under basic conditions, carbamate **36a** generates a free aza-*o*-xylylene upon losing CO_2.

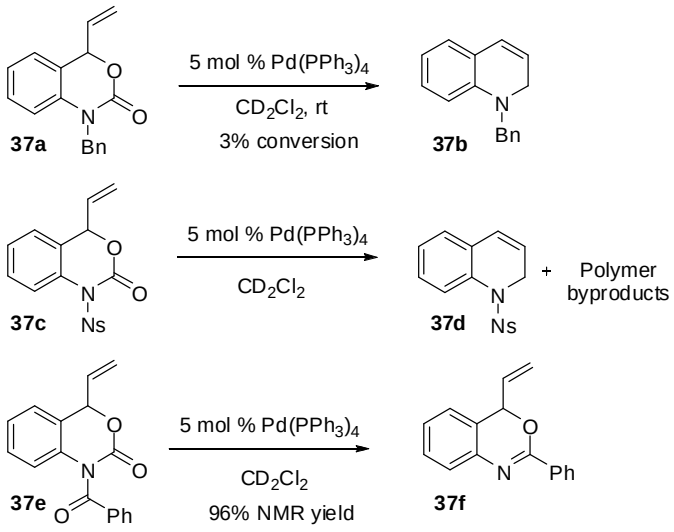
Scheme 33 *Problematic reactions*



Vinyl benzoxazinanones with different protecting groups were also prepared and subjected to the decarboxylative allylic amination under our standard reaction conditions (Scheme 34). It was found that benzyl-protected benzoxazinanone **37a** was not reactive, as expected considering that the decarboxylation is not favorable since

the pKa of the secondary amine is relatively high. The reaction only afforded a small amount of quinoline product **37b** (3% conversion), while most of starting material was recovered. When *N*-nosyl benzoxazinanone **37c** was allowed to react with 5 mol% $Pd(PPh_3)_4$, dihydroquinoline **37d** did form along with large amount of polymer-like byproduct. Benzoyl protected benzoxazinanone **37e** was also prepared and treated with the standard condition to generate the oxazine product **37f** in 96% NMR yield.

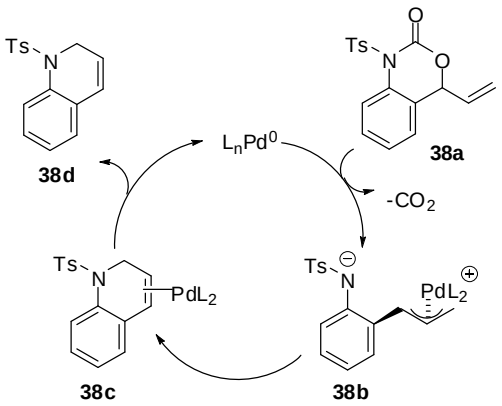
Scheme 34 *Vinyl benzoxazinanones with different protecting groups*



The formation of dihydroquinoline ring was thought to start by oxidative addition, followed by decarboxylation to generate a palladium-polarized aza-*ortho*-xylylene intermediate **38b**, followed by intramolecular allylic amination to product **38d** and regenerate the catalyst (Scheme 35). Due to unfavorable enthalpy of 4-membered ring

closure and bond angles, the 6-memered ring was favored as compared to the decarboxylative ring contraction of unsaturated analogues.

Scheme 35 *Catalytic cycle for decarboxylative dihydroquinoline synthesis via aza-ortho-xylylene intermediates*



In conclusion, we have developed a unique and efficient way for dihydroquinoline synthesis through palladium-polarized aza-*ortho*-xylylene intermediates. Interestingly, carrying out the same reactions in less polar solvents such as toluene produced a 12-membered dimer product cleanly, while reactions in more polar dichloromethane selectively produced dihydroquinolines. Importantly, the reactions proceed under mild conditions and produce CO_2 as the only byproduct.

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Appendix B

Experimental Procedures and Data for Chapter 2

General Experimental

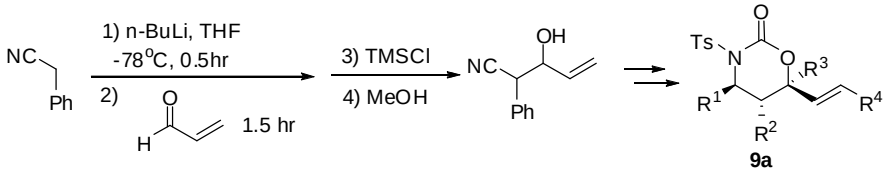
THF was dried over sodium metal. Toluene, methylene chloride and diethyl ether were dried over activated alumina on a solvent system purchased from Innovative Technology, Inc. Acetonitrile and 1,4-dioxane were dried and stored over activated molecular sieves. Commercially available reagents were used without additional purification unless otherwise stated. Products were purified on silica gel from Sorbent Technologies (230x400 mesh, 60 Å porosity, pH 6.5-7.5). Ruthenium and palladium compounds were obtained from Strem. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5715-7, EMD chemicals). UV lamp (254 nm) or $KMnO_4$ stain were used for monitoring TLC plates.

^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance 400 or Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals. Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, and HMQC spectroscopies and X-ray data. High resolution mass spectrometry was performed on an AUTOSPEC-Q tandem hybrid mass spectrometer (VG Analytical Ltd, Manchester, UK). High resolution mass spectrometry was performed on a LCT Premier (Waters Corp., Milford MA) time of flight mass spectrometer. FTIR spectra were acquired on a Shimadzu FTIR-8400S spectrometer. HPLC analysis was performed on a Shimadzu SCL-10A VP instrument.

Preparation of Starting Materials

Vinyl oxazinanone **9a**, in which R^1=H were prepared from the corresponding amino alcohols, which were synthesized by reduction of β-hydroxy nitriles with LAH.[1] β-Hydroxy nitriles were prepared by treatment of substituted nitriles with n-butyl lithium, followed by aldol reaction with the aldehydes. To increase the yield of aldol reaction, a modified procedure was used and 1.5 eq. of chloro trimethylsilane was added to trap the generated enolates, followed by methanol quenched.[2]

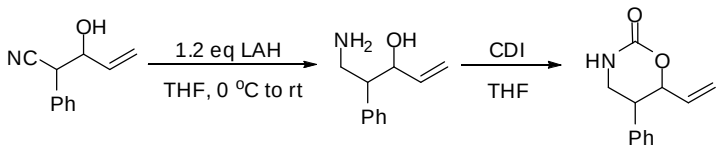
To a solution of n-butyl lithium (9.6 mmol, 1.1 eq.) in THF at -78 ^{o}C under argon was added benzyl cyanide (1.0 g, 8.7 mmol) dropwise, and the reaction mixture was stirred at -78 ^{o}C for 0.5 hour before adding a solution of acrolein (486 mg, 8.7 mmol, 1.0 eq.) in THF via cannulation. The reaction mixture turned pale yellow color upon addition and kept stirring at -78 ^{o}C until reaction completion indicated by TLC (generally 0.5 hr-1.5h). The reaction was quenched by chloro trimethylsilane (1.5 g, 13.1 mmol, 1.5 eq.), followed by adding methanol (2.0 ml). The reaction mixture was extracted by ethyl acetate, washed with brine, dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 5:1 Hexane: Ethyl acetate).[2]



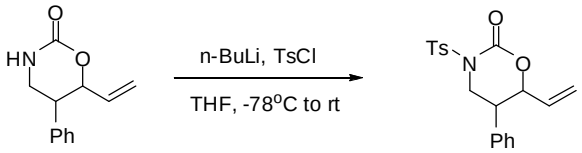
To a solution of LAH (290 mg, 7.6 mmol, 1.2 eq.) in THF under argon at 0 ^{o}C was slowly added a solution of cyano alcohol (1.1 g, 6.4 mmol) in THF via

cannulation. The resulting yellow mixture was kept stirring until reaction completion indicated by TLC (generally 0.5 hr). Because amino alcohols were very polar with a higher solubility in water, a slightly different work-up procedure was used. Small amount of water was added dropwise to the reaction mixture to quench the excess amount of LAH, which was monitored by the release of hydrogen, followed by adding ethyl acetate and filtration over a celite pad, dried over magnesium sulfate and the solvent was removed to afford the crude product which was taken to the next step without further purification. (One thing to note here is that the reduction step is very sensitive to water, and the solvent was dried over sodium metal before use.)

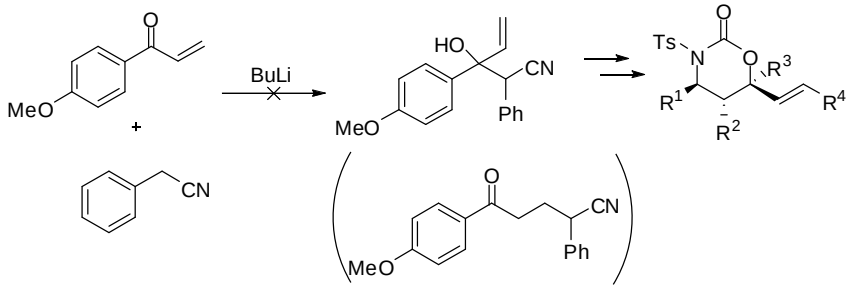
The preparation of carbamates was achieved by treatment of amino alcohols with CDI (carbonyl diimidazole) reagent.[3] The coupling step could also be performed stepwise by reacting with chloroformate, followed by an intramolecular cyclization under basic conditions.[4] To a solution of amino alcohol (1.1g, 5.2 mmol) in THF at room temperature was added carbonyl diimidazole (CDI, 923 mg, 5.7 mmol, 1.1 eq). The mixture was kept stirring at room temperature until reaction completion indicated by TLC (generally 12 hr). Most of the THF was removed, and the residue was taken up with ethyl acetate, washed with dilute hydrochloric acid, brined and dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 1:2 Hexane: Ethyl acetate).



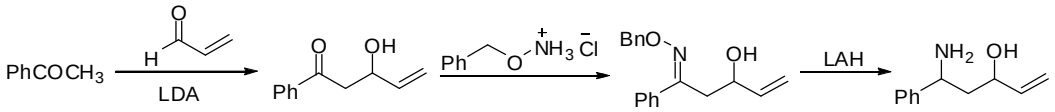
Finally, *N*-protected carbamates were prepared according to literature procedure.[5] Sodium hydride and n-butyl lithium were both used for deprotonation, though the latter one gave the product in better yield. To a solution of carbamate (300 mg, 2.1 mmol) in THF at -78 ^{o}C under argon was added n-BuLi (2.3 mmol, 1.1 eq.) dropwise, and stirred for 1.5 hr before the addition of TsCl (486 mg, 2.6 mmol, 1.2 eq.) in one portion. The yellow solution turned colorless upon addition of TsCl and monitored by TLC analysis. The reaction was quenched with sat. NH_4Cl solution after 0.5 hr, extracted with ethyl acetate. The organic phase was washed with brined, dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 1:5 Hexane: Ethyl acetate).



This method was not successful when R^2, R^3 are both aromatic rings, in which 1,4-addition was favored due to steric reasons.



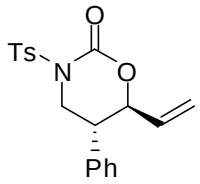
In the case of R^1=Ph, amino alcohol was efficiently synthesized from the corresponding adol adduct by a reductive amination protocol developed by Yamazaki.[6]



General procedure for catalytic decarboxylative ring contraction of vinyl oxazinanoes:

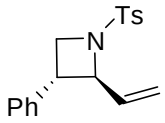
In a Schlenk tube under argon, $Pd(PPh_3)_4$ (0.05 mmol) and carbamate (1 mmol) were dissolved in 5 mL of methylene chloride. The resulting yellow solution was stirred at ambient temperature under Ar until reaction completion was indicated by TLC (generally 10 min.-2h). Following solvent evaporation, the crude product was purified via flash chromatography (SiO_2, 7:1 Hexane: Ethyl acetate).

Spectroscopic Data



5-phenyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one
10a (cw1293)
Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (d, 2H, *J* = 8.3 Hz: arom H), 7.31 - 7.43 (m, 4H: arom H), 7.21 (dd, 2H, *J*=7.7, 1.6 Hz: arom H), 5.62 (ddd, 1H, *J*=17.1, 10.7, 5.9 Hz: C**H**=), 5.27 (dt, 1H, *J*=17.1, 1.1 Hz: CH=C**H**$(H)_E$), 5.19 (dt, 1H, *J*=10.6, 1.0 Hz: CH=C**H**$(H)_Z$), 4.95 (dd, 1H, *J*=9.4, 5.8 Hz: OC**H**), 4.28 (dd, 1H, *J*=12.2, 5.2 Hz: diastereotopic C**H**$_2$NTs), 3.98 (dd, 1H, *J*=12.2, 10.5 Hz: diastereotopic C**H**$_2$NTs), 3.12 (td, 1H, *J*=9.9, 5.2 Hz: PhC**H**), 2.46 (s, 3H: C**H**$_3$).



3-phenyl-1-tosyl-2-vinylazetidine

13a(cw2028)

White solid

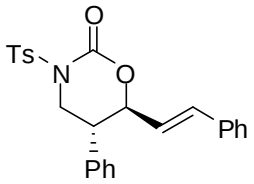
$Pd(PPh_3)_4$: 74% yield, dr = 16

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, 2H, *J* = 8.3 Hz: arom H), 7.43 (d, 2H, *J* = 7.8 Hz: arom H), 7.22 (m, 3H: arom H), 6.88 (m, 3H: arom H), 6.06 (m, 1H: =C**H**), 5.35 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 5.24 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_Z$), 4.35 (t, 1H, *J* =7.6 Hz: C**H**NTs), 4.06 (t, 1H, *J* =7.8 Hz: C**H**$_2$), 3.77 (t, 1H, *J* =8.1Hz: C**H**$_2$), 3.52 (q, 1H, *J* = 8.3, 16.4 Hz: PhC**H**), 2.51 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.52 (Quat.), 139.33 (Quat.), 136.96 (=**C**H), 132.92 (Quat.), 130.14 (Arom. **C**H), 129.05 (Arom. **C**H), 128.95 (Arom. **C**H), 127.63 (Arom. **C**H), 127.38 (Arom. **C**H), 118.24 (=**C**H$_2$), 72.74 (**C**HNTs), 54.44 (**C**H$_2$), 41.96 (**C**HPh), 21.95 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3088, 3065, 3032, 1599, 1495, 1346, 1165, 818, 669.

HRMS calcd for $C_{18}H_{20}NO_2S$ [M+H] 314.1215, found 314.1201.

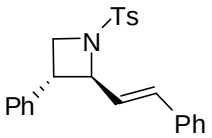


5-phenyl-6-styryl-3-tosyl-1,3-oxazinan-2-one

14a (cw2117)

Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (d, 1H, *J*=8.4 Hz: arom H), 7.34 (m, 6H: arom H), 7.22 (m, 6H: arom H), 6.54 (d, 1H, *J*=16.0 Hz: =C**H**Ph), 5.92 (dd, 1H, *J*=15.9, 6.3 Hz: C**H**=), 5.12 (ddd, 1H, *J*=9.5, 6.3, 1.2 Hz: OC**H**), 4.32 (dd, 1H, *J*=12.2, 5.2 Hz: diastereotopic C**H**$_2$NTs), 4.01 (dd, 1H, *J*=12.2, 10.6 Hz: diastereotopic C**H**$_2$NTs), 3.21 (td, 1H, *J*=10.0, 5.1 Hz: C**H**Ph), 2.46 (s, 3H: C**H**$_3$).



3-phenyl-2-styryl-1-tosylazetidine

13b (cw2121)

White solid

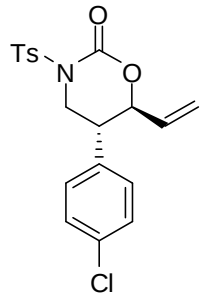
$Pd(PPh_3)_4$: 62% yield, dr = >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, 2H, *J* = 8.3 Hz: arom H), 7.44 (d, 2H, *J* = 7.8 Hz: arom H), 7.34 (m, 4.6H: arom H), 7.25 (m, 3.4H: arom H), 6.90 (m, 2H: arom H), 6.59 (d, 1H, *J* = 15.9 Hz: =C**H**Ph), 6.39 (dd, 1H, *J* = 7.1, 15.9 Hz: =C**H**), 4.50 (t, 1H, *J* =7.3 Hz: C**H**NTs), 4.12 (t, 1H, *J* =8.3 Hz,: C$\mathbf{H}_2$), 3.83 (t, 1H, *J* =8.3Hz: C$\mathbf{H}_2$), 3.61 (q, 1H, *J* = 8.3, 16.2 Hz: PhC**H**), 2.49 (s, 3H: C$\mathbf{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.74 (Quat.), 139.26 (Quat.), 136.44 (Quat.), 133.31 (=**C**HPh), 132.61 (Quat.), 130.27-127.19 (overlapping Arom. **C**H, =**C**H), 72.94 (**C**HNTs), 54.37 (**C**H_2), 42.56 (**C**HPh), 22.05 (**C**H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3084, 3065, 3032, 1599, 1495, 1346, 1163, 966, 816, 750, 669.

HRMS calcd for $C_{24}H_{24}NO_2S$ [M+H] 390.1528, found 390.1547.



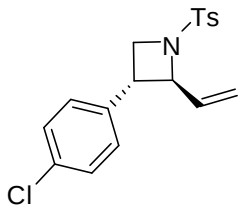
5-(4-chlorophenyl)-3-tosyl-6-vinyl-1,3-oxazinan-2-one

12a (cw2098)

Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.88 (d, 2H, *J*=8.3 Hz: arom H), 7.34 (t, 4H, *J*=7.0 Hz: arom H), 7.14 (m, 2H: arom H), 5.61 (ddd, 1H, *J*=17.0, 10.7, 5.9 Hz: C**H**=), 5.27 (d, 1H, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 5.22 (d, 1H, *J*=10.5 Hz: CH=C**H**(*H*)$_Z$), 4.91 (m, 1H: OC**H**), 4.25 (dd, 1H, *J*=12.3, 5.1 Hz: diastereotopic C$\mathbf{H}_2$NTs), 3.95 (m, 1H: diastereotopic C$\mathbf{H}_2$NTs), 3.12 (ddd, 1H, *J*=9.5, 4.9, 4.8 Hz: ArC**H**), 2.47 (s, 3H: C$\mathbf{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 148.5 (N**C**O_2), 145.8 (Quat.), 135.2 (Quat.), 134.6 (Quat.), 133.6 (Quat.), 130.8 (**C**H=), 129.9 (Arom. **C**H), 129.8 (Arom. **C**H), 129.6 (Arom. **C**H), 129.3 (Arom. **C**H), 120.5 (=**C**H_2), 81.2 (O**C**H), 47.8 (**C**H_2NTs), 41.0 (Ar**C**H), 22.2 (**C**H_3).



3-(4-chlorophenyl)-1-tosyl-2-vinylazetidine

13e (cw2100)

colorless oil

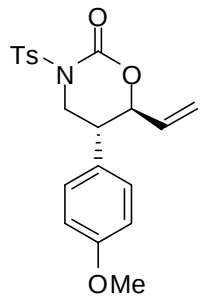
$Pd(PPh_3)_4$: 78% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, 2H, *J* = 8.3 Hz: arom H), 7.44 (d, 2H, *J* = 8.1 Hz: arom H), 7.20 (d, 2H, *J* = 8.6Hz: arom H), 6.76 (d, 2H, *J* = 8.6Hz: arom H), 6.03 (m, 1H: =C**H**), 5.32 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 5.23 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_Z$), 4.25 (t, 1H, *J* =7.1 Hz: C**H**NTs), 4.05 (t, 1H, *J* =8.1 Hz: C**H**$_2$), 3.69 (t, 1H, *J* =8.4Hz: C**H**$_2$), 3.48 (q, 1H, *J* =8.3, 16.4 Hz: ArC**H**), 2.52 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.36 (Quat.), 137.35 (Quat.), 136.24 (=**C**H), 133.28 (Quat.), 131.97 (Quat.), 129.86-128.37 (Arom. **C**H), 118.27 (=**C**H_2), 72.47 (**C**HNTs), 53.97 (**C**H_2), 40.91 (**C**HAr), 21.68 (**C**H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3087, 3031, 1600, 1495, 1348, 1165, 1094, 820, 669.

HRMS calcd for $C_{18}H_{19}ClNO_2S$ [M+H] 348.0825, found 348.0820.

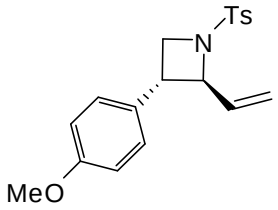


5-(4-methoxyphenyl)-3-tosyl-6-vinyl-1,3-oxazinan-2-one

cw2136

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, 1H, *J*=8.5 Hz: arom H), 7.34 (d, 1H, *J*=8.1Hz: arom H), 7.12 (d, 1H, *J*=8.8 Hz: arom H), 6.91 (d, 1H, *J*=8.7 Hz: arom H), 5.61 (ddd, 1H, *J*=16.9, 10.7, 5.8 Hz: C**H**=), 5.27 (d, 1H, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 5.19 (d, 1H, *J*=10.6 Hz: CH=C**H**(*H*)$_Z$), 4.90 (dd, 1H, *J*=9.5, 5.8 Hz: OC**H**), 4.25 (dd, 1H, *J*=12.2, 5.3 Hz: diastereotopic C**H**$_2$NTs), 3.93 (dd, 1H, *J*=12.2, 10.7 Hz: diastereotopic C**H**$_2$NTs), 3.83 (s, 3H: OC**H**$_3$), 3.07 (td, 1H, *J*=10.0, 5.2 Hz: ArC**H**), 2.47 (s, 3H: C**H**$_3$).



3-(4-methoxyphenyl)-1-tosyl-2-vinylazetidine

13f (cw2140)

White solid

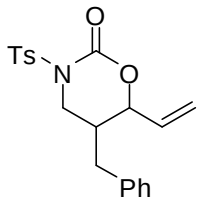
$Pd(PPh_3)_4$: 84% yield, dr = 14:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, 2H, *J* = 8.3 Hz: arom H), 7.42 (d, 2H, *J* = 8.6 Hz: arom H), 7.22 (m, 3H: arom H), 6.75 (s, 4H: arom H), 6.04 (m, 1H: =C**H**), 5.26 (dd, 2H, *J* = 10.4, 16.9 Hz: =C**H**$_2$), 4.24 (t, 1H, *J* =7.1 Hz: C**H**NTs), 4.04 (t, 1H, *J* =7.8 Hz: C**H**$_2$), 3.77 (s, 3H: OC**H**$_3$), 3.68 (t, 1H, *J* =7.8Hz: C**H**$_2$), 3.46 (q, 1H: ArC**H**), 2.52 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.25 (Quat.), 144.60 (Quat.), 136.91 (=**C**H), 132.41 (Quat.), 131.26 (Quat.), 130.22-128.56 (Arom. **C**H), 118.26 (=**C**H$_2$), 114.42 (Arom. **C**H), 73.26 (**C**HNTs), 55.68 (O**C**H$_3$), 54.89 (**C**H$_2$), 41.42 (**C**HAr), 22.07 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3065, 3005, 1516, 1466, 1346, 1250, 1165, 829, 818.

HRMS calcd for $C_{19}H_{22}NO_3S$ [M+H] 344.1320, found 344.1315.

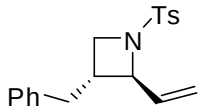


5-benzyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one

12c (cw2164)

White solid, dr = 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (t, 4H, *J*=8.4 Hz: arom H (cis/trans)), 7.34 (m, 10H: arom H (cis/trans)), 7.15 (dd, 4H, *J*=16.9, 7.0 Hz: arom H (cis/trans)), 5.91 (td, 1H, *J*=11.3, 5.4 Hz: =C**H** (cis/trans)), 5.81 (ddd, 1H, *J*=17.0, 10.8, 5.9 Hz: =C**H** (cis/trans)), 5.38 (m, 4H: =C**H**$_2$ (cis/trans)), 4.61 (t, 1H: OC**H** (cis/trans)), 4.83 (br. s., 1H: OC**H** (cis/trans)), 3.88 (dd, 1H, *J*=12.2, 4.8 Hz: C**H**$_2$NTs (cis/trans)), 3.69 (ddd, 1H, *J*=11.9, 7.5, 7.4 Hz: C**H**$_2$NTs (cis/trans)), 2.90 (dd, 1H, *J*=14.0, 5.9 Hz: C**H**$_2$Ph (cis/trans)), 2.78 (d, 1H, *J*=7.8 Hz: C**H**$_2$Ph (cis/trans)), 2.56 (m, 3H: overlapping C**H**$_2$Ph, BnC**H** (cis/trans)), 2.47 (s, 3H: C**H**$_3$ (cis/trans)), 2.46 (s, 3H: C**H**$_3$ (cis/trans)), 2.28 (m, 1H: BnC**H** (cis/trans)).



3-benzyl-1-tosyl-2-vinylazetidine

13g (cw2170)

White solid

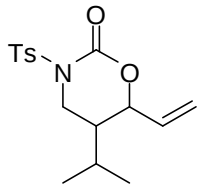
$Pd(PPh_3)_4$: 60% yield, dr = 8.5

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H: arom H), 7.37 (d, *J* =8.6 Hz, 2H: arom H), 7.23 (m, 3H: arom H), 7.25 (d, *J* = 7.1 Hz, 2H: arom H), 5.85 (m, 1H: =C**H**), 5.14 (dd, *J* = 9.8, 17.7 Hz, 1H: =C**H**$_2$), 4.04 (t, 1H, *J* =6.8 Hz: C**H**NTs), 3.78 (t, *J* =7.8 Hz, 1H: C**H**$_2$NTs), 3.36 (t, *J* =7.6Hz, 1H: C**H**$_2$NTs), 2.62 (m, 1H: BnC**H**), 2.50 (m, 5H: overlapping C**H**$_2$, C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.42 (Quat.), 138.26 (Quat.), 137.02 (=**C**H), 132.62 (Quat.), 130.07-126.93 (Arom. **C**H), 117.74 (=**C**H$_2$), 70.47 (**C**HNTs), 53.45 (**C**H$_2$NTs), 38.97 (**C**H$_2$Ph), 38.31 (**C**HBn), 22.08 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3086, 3065, 3030, 1599, 1497, 1344, 1165, 816, 669.

HRMS calcd for $C_{19}H_{22}NO_2S$ [M+H] 328.1371, found 328.1360.

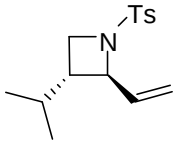


5-isopropyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one

12d (cw3099)

White solid, dr = 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (t, 4H, *J*=7.8 Hz: arom H (cis/trans)), 7.35 (d, 4H: arom H (cis/trans)), 5.81 (m, 2H: =C**H** (cis/trans)), 5.34 (m, 4H: =C**H**$_2$ (cis/trans)), 4.93 (br. s., 1H: OC**H** (cis/trans)), 4.72 (t, 1H, *J*=6.5 Hz: OC**H** (cis/trans)), 4.12 (ddd, 1H, *J*=11.7, 5.3, 1.6 Hz: C**H**$_2$NTs (cis/trans)), 3.93 (m, 1H: C**H**$_2$NTs (cis/trans)), 3.84 (m, 1H: C**H**$_2$NTs (cis/trans)), 3.48 (t, 1H, *J*=11.9 Hz: C**H**$_2$NTs (cis/trans)), 2.46 (s, 6H: C**H**$_3$Ts (cis/trans)), 1.91 (m, 2H: overlapping C**H**$(CH_3)_2$, C**H**CH_2NTs (cis/trans)), 1.78 (m, 1H: overlapping C**H**$(CH_3)_2$, C**H**CH_2NTs (cis/trans)), 1.59 (m, 1H: overlapping C**H**$(CH_3)_2$, C**H**CH_2 (cis/trans)), 1.06 (m, 8H: C**H**$_3$ (cis/trans)), 0.99 (d, 4H, *J* = 6.8 Hz: C**H**$_3$ (cis/trans)).



3-isopropyl-1-tosyl-2-vinylazetidine

13h (cw2239)

colorless oil

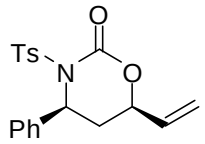
$Pd(PPh_3)_4$: 93% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H: arom H), 7.38 (d, *J* =8.1 Hz, 2H: arom H), 5.85 (m, 1H: =C**H**), 5.33 (d, *J* = 16.9 Hz, 1H: =C**H**$_2$(*H*)$_E$), 5.18 (d, *J* = 10.4 Hz, 1H: =C**H**$_2$(*H*)$_Z$), 3.95 (t, 1H, *J* =7.1 Hz: C**H**NTs), 3.74 (t, *J* =7.8 Hz, 1H: C**H**$_2$NTs), 3.24 (t, *J* =7.8Hz, 1H: C**H**$_2$NTs), 2.46 (s, 3H: C**H**$_3$(Ts)), 2.01 (m, 1H: C**H**), 1.29 (m, 1H: C**H**$(CH_3)_2$), 0.72 (d, *J* =6.6Hz, 3H: C**H**$_3$), 0.68 (d, *J* =6.6Hz, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.31 (Quat.), 137.99 (=**C**H), 130.03 (Quat.), 130.03 (Arom. **C**H), 128.75 (Arom. **C**H), 117.68 (=**C**H_2), 70.12 (**C**HNTs), 52.51 (**C**H_2NTs), 44.20 (**C**H), 32.51 (**C**H$(CH_3)_2$), 22.03 (**C**H_3(Ts)), 19.71/19.59 (**C**H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC, NOESY etc.

FTIR ($CDCl_3$): ν_{max} 3053, 1599, 1495, 1344, 1163, 818, 671.

HRMS calcd for $C_{15}H_{21}NO_2SNa$ [M+Na] 302.1191, found 302.1191.

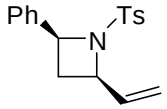


4-phenyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one

17a (cw2212)

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.23 - 7.37 (m, 5H: arom H), 7.15 (d, 2H, *J*=7.8 Hz: arom H), 7.04 (d, 2H, *J*=8.6 Hz: arom H), 5.84 (ddd, 1H, *J*=17.1, 10.8, 5.9 Hz: C**H**=), 5.47 (m, 2H: overlapping CH=C**H**(*H*)$_E$ and C**H**Ph), 5.32 (d, 1H, *J*=10.6 Hz: CH=C**H**(*H*)$_Z$), 4.91 (dd, 1H, *J*=11.3, 5.9 Hz: OC**H**), 2.63 (ddd, 1H, *J*=14.4, 8.1, 1.9 Hz: diastereotopic C**H**$_2$), 2.36 (s, 3H: C**H**$_3$), 2.04 (dt, 1H, *J*=14.4, 11.0 Hz: diastereotopic C**H**$_2$).



2-phenyl-1-tosyl-4-vinylazetidine

13i (cw2221)

colorless oil

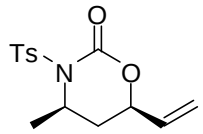
$Pd(PPh_3)_4$: 92% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H: arom H), 7.42 (d, *J* = 7.1 Hz, 2H: arom H), 7.33 (m, 5H: arom H), 6.06 (m, 1H: =C**H**), 5.38 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 5.25 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_Z$), 4.81 (t, 1H, *J* =8.3 Hz: PhC**H**), 4.41 (q, *J* =8.1, 4.9 Hz, 1H: C**H**CH=CH$_2$), 2.61 (d t, *J* =8.3, 10.9 Hz, 1H: C**H**$_2$), 2.45(s, 3H: C**H**$_3$), 1.99(d t, *J* =8.3, 10.9 Hz, 1H: C**H**$_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.05 (Quat.), 141.05 (Quat.), 137.92 (=**C**H), 133.46 (Quat.), 130.02-126.96 (Arom. **C**H), 117.71 (=**C**H$_2$), 62.66 (Ph**C**H), 66.19 (**C**HCH=CH$_2$), 33.68 (**C**H$_2$), 22.02 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC, NOESY etc.

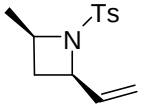
FTIR ($CDCl_3$): ν_{max} 3087, 3066, 3031, 1599, 1495, 1346, 1163, 816, 748, 665.

HRMS calcd for $C_{18}H_{20}NO_2S$ [M+H] 314.1215, found 314.1216; $C_{18}H_{19}NO_2SNa$ [M+Na] 336.1034, found 336.1048.



4-methyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one
cw2243
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.99 (d, 2H, *J*=8.7 Hz: arom H), 7.33 (dd, 2H, *J*=8.1, 0.6 Hz: arom H), 5.84 (ddd, 1H, *J*=17.2, 10.7, 5.6 Hz: C**H**=), 5.40 (dd, 1H, *J*=17.2, 0.9 Hz: CH=C**H**(*H*)$_E$), 5.29 (d, 1H, *J*=10.7 Hz: CH=C**H**(*H*)$_Z$), 4.66 (m, 2H: overlapping C**H**CH_3 and OC**H**), 2.45 (m, 4H: overlapping C**H**$_3$NTs and diastereotopic C**H**$_2$), 1.77 (dt, 1H, *J*=14.1, 9.7 Hz: diastereotopic C**H**$_2$), 1.49 (s, 3H: C**H**$_3$).



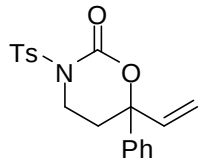
2-methyl-1-tosyl-4-vinylazetidine
13j (cw2247)
White solid
$Pd(PPh_3)_4$: 78% yield, dr = 8:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H: arom H), 7.36 (d, *J* =7.8 Hz, 2H: arom H), 5.95 (m, 1H: =C**H**), 5.26 (td, *J* = 1.3, 17.2 Hz, 1H: =C**H**$_2$(*H*)$_E$), 5.14 (d, *J* =1.3, 10.4 Hz, 1H: =C**H**$_2$(*H*)$_Z$), 4.11 (q, 1H, *J* =8.1, 15.2 Hz: C**H**NTs), 3.82 (m, 1H: C**H**CH_3), 2.46 (s, 3H: C**H**$_3$(Ts)), 2.26 (m, 1H: C**H**$_2$), 1.68 (m, 1H: C**H**$_2$), 1.40 (d, *J* =6.3 Hz, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.85 (Quat.), 137.94 (=**C**H), 132.66 (Quat.), 129.65 (Arom. **C**H), 128.34 (Arom. **C**H), 116.91 (=**C**H_2), 61.47 (**C**HNTs), 56.68 (**C**HCH_3), 31.68 (**C**H_2), 22.56 (**C**H_3), 21.61 (**C**H_3(Ts)),. The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC, NOESY etc.

FTIR ($CDCl_3$): ν_{max} 3055, 1600, 1495, 1342, 1163, 818.

HRMS calcd for $C_{13}H_{18}NO_2S$ [M+H] 252.1058, found 252.1056.

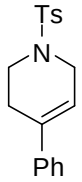


6-phenyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one

15a (cw2223)

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.80 (dd, 2H, *J*=8.3, 1.5 Hz: arom H), 7.31 (m, 7H: arom H), 6.02 (ddd, 1H, *J*=17.2, 10.8, 1.4 Hz: C**H**=), 5.26 (dd, 1H, *J*=7.4, 1.4 Hz: CH=C**H**(*H*)$_Z$), 5.24 (dd, 1H, *J*=13.9, 1.3 Hz: CH=C**H**(*H*)$_E$), 3.96 (dddd, 1H, *J*=12.0, 6.8, 5.2, 1.2 Hz: diastereotopic C**H**$_2$NTs), 3.75 (m, 1H: diastereotopic C**H**$_2$NTs), 2.47 (m, 5H: overlapping: C**H**$_3$ and C**H**$_2$).



4-phenyl-1-tosyl-1,2,3,6-tetrahydropyridine

15b (cw2226)

White solid

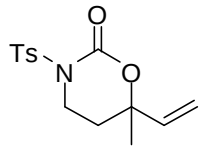
$Pd(PPh_3)_4$: 99% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H: arom H), 7.34 (m, 7H: arom H), 5.98 (broad s, 1H: =C**H**), 3.78 (broad s, 2H: =HCC**H**$_2$NTs), 3.34 (t, 2H, *J* =5.6 Hz: TsNC**H**$_2$), 2.64 (broad s, 2H: C**H**$_2$), 2.46 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.10 (Quat.), 140.50 (Quat.), 135.76 (Quat.), 133.42 (Quat.), 130.12-125.40 (Arom. **C**H), 119.40 (=**C**H), 45.69 (=HC**C**H$_2$NTs) 43.45 (**C**H$_2$NTs), 27.96 (**C**H$_2$), 21.98 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3065, 3033, 1597, 1495, 1342, 1167, 816, 673.

HRMS calcd for $C_{18}H_{20}NO_2S$ [M+H] 314.1215, found 314.1212.

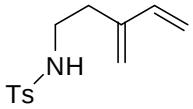


6-methyl-3-tosyl-6-vinyl-1,3-oxazinan-2-one

15c (cw2189)

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (d, 2H, *J*=8.1 Hz: arom H), 7.38 (d, 2H, *J*=8.4 Hz: arom H), 5.82 (ddd, 1H, *J*=17.2, 10.9, 0.8 Hz: C**H**=), 5.21 (d, 1H, *J*=10.9 Hz: CH=C**H**(*H*)$_Z$), 5.08 (d, 1H, *J*=17.2 Hz: CH=C**H**(*H*)$_E$), 4.07 (dt, 1H, *J*=11.9, 4.6 Hz: diastereotopic C**H**$_2$NTs), 3.73 (td, 1H, *J*=11.8, 5.0 Hz: diastereotopic C**H**$_2$NTs), 2.48 (s, 3H: C**H**$_3$Ts), 2.07 (m, 2H: C**H**$_2$), 1.45 (s, 3H: C**H**$_3$).



4-methyl-*N*-(3-methylenepent-4-enyl)benzenesulfonamide

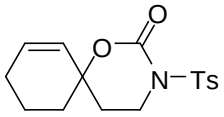
15d (cw2201)

colorless oil

$Pd(PPh_3)_4$: 40% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H: arom H), 7.33 (d, *J* = 8.5 Hz, 2H: arom H), 6.29 (dd, 1H, *J*=17.7, 10.8 Hz: C**H**=CH_2), 4.92-5.19 (m, 4H: overlapping =C**H**$_2$), 4.50 (s, 1H: N**H**Ts), 3.12 (q, *J*=6.7 Hz, 2H: C**H**$_2$NHTs), 2.45 (s, 3H: C**H**$_3$Ts). 2.41 (t, 2H, *J*=6.9 Hz: C**H**$_2$)

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.85 (Quat.), 142.57 (Quat.), 138.10 (**C**H=), 137.37 (Quat.), 130.13 (Arom. **C**H), 127.53 (Arom. **C**H), 118.57 (overlapping =**C**H_2), 114.65 (overlapping =**C**H_2), 41.82 (**C**H_2NHTs), 21.98 (**C**H_3), 31.93 (**C**H_2).



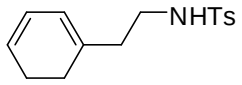
3-tosyl-1-oxa-3-azaspiro[5.5]undec-7-en-2-one

15e (cw2122)

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.95 (d, 2 H, *J*=8.3 Hz: arom H), 7.34 (dt, 2H, *J*=8.0, 0.7 Hz: arom H), 6.02 (ddd, 1H, *J*=10.1, 4.2, 3.2 Hz: =C**H**CH_2), 5.62 (d, 1 H, *J*=10.2 Hz: =C**H**), 4.02 (ddd, 2H, *J*=6.8, 6.0, 1.2 Hz: C**H**$_2$NHTs), 2.45 (s, 3 H: C**H**$_3$),

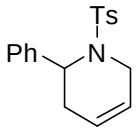
2.05 (m, 5H: overlapping C**H**$_2$), 1.87 (m, 1H: overlapping C**H**$_2$), 1.67 (m, 2H: overlapping C**H**$_2$).



N-(2-(cyclohexa-1,3-dienyl)ethyl)-4-methylbenzenesulfonamide
15f (cw2129)
colorless oil
Pd(PPh$_3$)$_4$: 99% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (d, 2H, *J*=8.3 Hz: arom H), 7.32 (d, 2H, *J*=8.6 Hz: arom H), 5.82 (m, 1H: =C**H**CH$_2$), 5.65 (d, 1H, *J*=9.6 Hz: C**H**=), 5.47 (br. s., 1H: C**H**=C(Quat.)), 4.46 (s, 1H: N**H**Ts), 3.02 (q, 2H, *J*=6.1 Hz: C**H**$_2$NHTs), 2.45 (s, 3H, overlapping C**H**$_2$), 2.16 (t, 3H, *J*=6.7 Hz: overlapping C**H**$_2$), 2.08 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.80 (Quat.), 137.27 (Quat.), 132.00 (Quat.), 130.11 (Arom. **C**H), 128.52 (**C**H=), 127.54 (Arom. **C**H), 126.02 (**C**H=), 123.89 (**C**H=), 41.74 (**C**H$_2$NHTs), 35.55 (**C**H$_2$), 22.62 (**C**H$_2$), 22.58 (**C**H$_2$), 21.98 (**C**H$_3$).



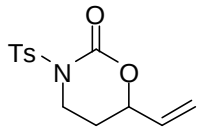
2-phenyl-1-tosyl-1,2,3,6-tetrahydropyridine
17b (cw2222)
White solid
Pd(PPh$_3$)$_4$: 68% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8, 2H: arom H), 7.38 (d, *J* = 8.3, 2H: arom H), 7.29 (m, 5H: arom H), 5.81 (m, 1H: PhCHCH$_2$=C**H**), 5.61 (m, 1H, =C**H**), 5.32 (br d, 1H, *J* =5.6 Hz: PhC**H**), 4.14 (br d , *J* =17.7 Hz, 1H: C**H**$_2$NTs), 3.42 (br d, *J* =19.7 Hz, 1H: C**H**$_2$NTs), 2.43 (5H: overlapping C**H**$_2$CHPh, C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.51 (Quat.), 139.58 (Quat.), 138.12 (Quat.), 129.95-127.43 (Arom. **C**H), 124.32 (PhCHCH$_2$=**C**H), 124.13 (=**C**H), 53.21 (Ph**C**H) 41.21 (**C**H$_2$NTs), 26.76 (**C**H$_2$), 21.95 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

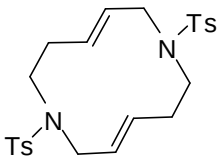
FTIR ($CDCl_3$): ν_{max} 3065, 3040, 1599, 1494, 1344, 1161, 816, 654.

HRMS calcd for $C_{18}H_{20}NO_2S$ [M+H] 314.1215, found 314.1219; $C_{18}H_{19}NO_2SNa$ [M+Na] 336.1034, found 336.1038.



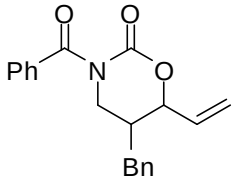
3-tosyl-6-vinyl-1,3-oxazinan-2-one
18a (cw2152)
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.04 (d, 1H, *J*=8.4 Hz: arom H), 7.36 (d, 1H, *J*=8.0 Hz: arom H), 5.83 (ddd, 1H, *J*=17.2, 10.7, 5.3 Hz: C**H**=), 5.32 (m, 1H: =C**H**$_2$), 4.84 (m, 1H: OC**H**), 4.08 (dt, 1H, *J* =12.0, 5.3 Hz: C**H**$_2$NTs), 3.91 (d, 1H, *J*=12.0, 9.5, 4.9 Hz: C**H**$_2$NTs), 2.46 (s, 3H: C**H**$_3$), 2.25 (m, 1H: C**H**$_2$), 1.98 (m, 1H: C**H**$_2$).



(4*E*,10*E*)-1,7-ditosyl-1,7-diazacyclododeca-4,10-diene
18c (cw2180)
White solid
$Pd(PPh_3)_4$: 26% yield

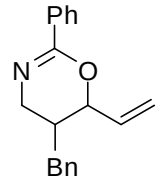
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.72 (d, 4H, *J*=8.3 Hz: arom H), 7.72 (d, 4H, *J*=8.6 Hz: arom H), 5.62 (dt, 1H, *J* =15.6, 6.8 Hz: C**H**=), 5.45 (dt, 1H, *J* =15.4, 5.8 Hz: C**H**=), 3.58 (d, 4H, *J*=5.8 Hz: C**H**$_2$NTs), 3.20 (m, 4H: C**H**$_2$=), 2.45 (s, 6H: C**H**$_3$), 2.41 (m, 4H: C**H**$_2$).



3-benzoyl-5-benzyl-6-vinyl-1,3-oxazinan-2-one
19a (cw2166)
White solid, dr = 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.20 - 7.59 (m, 10H: arom H (cis/trans)), 6.10 (m, 1H: =C**H** (cis/trans)), 5.97 (m, 1H: =C**H** (cis/trans)), 5.55 (m, 4H: =C**H**$_2$ (cis/trans)), 4.95 (br. s., 1H: OC**H** (cis/trans)), 4.74 (br. s., 1H: OC**H** (cis/trans)), 3.96 (d, 1H, *J*=13.3 Hz: C**H**$_2$NTs (cis/trans)), 3.88 (ddd, 1H, *J*=12.8, 5.4, 4.2 Hz: C**H**$_2$NTs (cis/trans)), 3.59 (m, 2H: C**H**$_2$NTs (cis/trans)), 3.02 (ddd, 1H, *J*=13.9, 4.5, 4.3 Hz: overlapping C**H**$_2$Ph, C**H**Bn (cis/trans)), 2.83 (m, 1H: overlapping C**H**$_2$Ph, C**H**Bn

(cis/trans)), 2.66 (m, 3H: overlapping C**H**$_2$Ph, C**H**Bn (cis/trans)), 2.39 (m, 1H: overlapping C**H**$_2$Ph, C**H**Bn (cis/trans)).



5-benzyl-2-phenyl-6-vinyl-5,6-dihydro-4*H*-1,3-oxazine

19b (cw2179)

White solid

Pd(PPh$_3$)$_4$: 60% yield, dr = 1.5:1

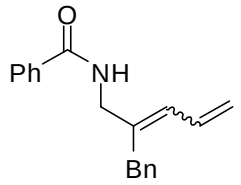
^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ ppm 8.00 (m, 2 H: arom H, overlapping minor/major isomers), 7.44 (m, 3 H: arom H, overlapping minor/major isomers), 7.33 (m, 2 H: arom H, overlapping minor/major isomers), 7.26 (m, 3 H: arom H, overlapping minor/major isomers), 6.00 (m,1 H, overlapping minor/major isomer: C**H**=), 5.40 (m, 2 H: =C**H**$_2$), 4.60 (t, 1 H, *J*=5.9 Hz: OC**H**), 3.59 (dd, 1 H, d, *J*=16.8, 4.9 Hz: C**H**$_2$N), 3.37 (td, 1 H, *J*=16.6, 8.1 Hz: C**H**$_2$N), 2.94 (dd, 1 H, *J*=13.6, 6.3 Hz: C**H**$_2$Ph), 2.58 (m, 1 H: C**H**$_2$Ph), 2.08 (m, 1 H: C**H**Bn).

Minor diastereoisomer: δ ppm 8.00 (m, 2 H: arom H, overlapping minor/major isomers), 7.44 (m, 3 H: arom H, overlapping minor/major isomers), 7.33 (m, 2 H: arom H, overlapping minor/major isomers), 7.26 (m, 3 H: arom H, overlapping minor/major isomers), 6.00 (m,1 H, overlapping minor/major isomer: C**H**=), 5.40 (m, 2 H: =C**H**$_2$), 4.87 (t, 1 H, *J*=3.7 Hz: OC**H**), 3.59 (dd, 1 H, d, *J*=16.8, 4.9 Hz: C**H**$_2$N), 3.37 (td, 1 H, *J*=16.6, 8.1 Hz: C**H**$_2$N), 2.68 - 2.73 (m, 1 H: C**H**$_2$Ph), 2.58 (m, 1 H: C**H**$_2$Ph), 2.43 (m, 1 H: C**H**Bn).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 155.14 (**C**=N), 139.55 (**C**=N), 139.40 (Quat.), 136.43 (**C**H=), 134.15 (Quat.), 133.60 (**C**H=), 126.81-130.85 (Arom. **C**H), 118.75 (=**C**H$_2$), 118.30 (=**C**H$_2$), 78.94 (O**C**H), 77.67 (O**C**H), 46.29 (**C**H$_2$N), 37.37 (**C**HBn), 37.26 (**C**HBn), 37.05 (**C**H$_2$Ph), 34.66 (**C**H$_2$Ph) (1.5:1 diastereomixture). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3062, 3030, 2926, 1657, 1581, 1495, 1117.

HRMS calcd for $C_{19}H_{20}NO$ [M+H] 278.1545, found 278.1527.



N-(2-benzylpenta-2,4-dienyl)benzamide

19c (cw2182)

colorless oil

$Pd(PPh_3)_4$: 96% NMR yield, dr =1.1:1

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ ppm 7.72 (m, 3H: arom H), 7.53 (m, 4H: arom H), 6.98 - 7.19 (m, 3 H: arom H), 6.66 (m, 1H: C**H**=), 6.01 (d, 1H, *J*=11.1 Hz: BnC=C**H**), 5.68 (br. s., 1H: N**H**), 5.15 (m, 2H; =C**H**$_2$), 3.99 (d, 2H, *J*=5.6 Hz: C**H**$_2$NH), 3.42 (s, 2H: C**H**$_2$Ph).

Minor diastereoisomer: δ ppm 7.72 (m, 3H: arom H), 7.53 (m, 4H: arom H), 6.98 - 7.19 (m, 3 H: arom H), 6.77 (m, 1H: C**H**=), 6.14 (d, 1H, *J*=11.1 Hz: BnC=C**H**), 5.68 (br. s., 1H: N**H**), 5.15 (m, 2 H; =C**H**$_2$), 4.18 (d, 2H, *J*=5.6 Hz: C**H**$_2$N), 3.99 (s, 2H: C**H**$_2$Ph).

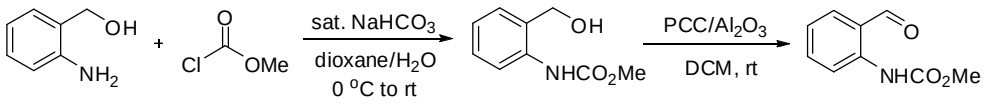
General procedure for synthesizing starting vinyl benzoxazinanones:

Amino benzalehydes were synthesized by oxidation of the corresponding amino alcohols except commercially available ones. *N*-protected carbamates were prepared from amino aldehydes by literature methods, followed by tosylation. ^{1}H NMR spectra were referenced to residual protio solvent signals. Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, HMQC.

Substituted *ortho*-amino benzyl alcohols were treated with chloroformate to synthesize the corresponding carbamates,[7] which were oxidized to aldehydes with PCC (pyridinium chlorochromate).[8] Grinard Reaction of the aldehydes,[9] followed by intramolecular cyclization upon treatment with potassium carbonate,[10] generated the desired vinyl benzoxazinanones in high yield. Finally, *N*-tosylation gave the starting material according to literature procedure.[11] One thing to note here is that all the above procedures generate the desired products in high yield and purity. Consequently, the only necessary flash column separation was the tosylation step, just to ensure the high purity of the starting material for Pd-catalyzed decarboxylative dihydroquinoline syntheses and asymmetric cycloadditions.

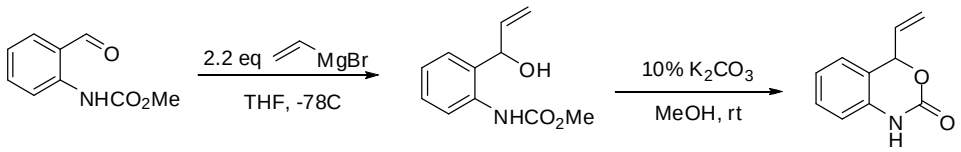
To a solution of amino alcohol (2.9 g, 23 mmol) in 14 ml 1,4-dioxane, 14 ml saturated $NaHCO_3$ and 5 ml of water at 0 ^{o}C, was added dropwise methyl chloroformate (2.2 ml, 1.2 eq.), and the reaction mixture was warmed up slowly to room temperature and stirred overnight. The reaction was quenched by brine, extracted by ethyl acetate, dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 2:1

Hexane: Ethyl acetate).[2] The oxidiation was carried out with PCC (pyridinium chlorochromate) preabsorbed on Al_2O_3. To a solution of carbamate (1.0 g, 5.5 mmol) in 30 ml dichloromethane at rt was added PCC/Al_2O_3 (8.3 mmol, 1.2 eq.) in one portion. The reaction mixture was kept stirring until reaction completion indicated by TLC (generally 2 hr). 50 ml of ether was poured in the reaction mixture and the resulting solution was filter through a pad of Florisil. The reaction flask was rinse three times and the organic phase was combined and the solvent was removed to give the amino aldehyde in 94% yield, which is pure enough for the next step reaction. (One thing to note here is that longer oxidation time lowers the yield)

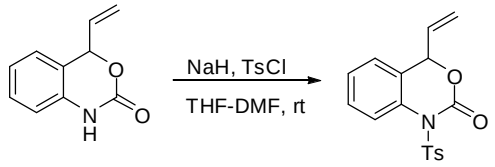


To a solution of amino aldehyde (450 mg, 2.5 mmol) in THF under argon at -78 ^oC was slowly added Grinard reagent (5.5 mmol, 2.2 eq.). The resulting yellow mixture was kept stirring at -78 ^oC for 2hrs before quenched with saturated NH_4Cl solution. The crude product was extracted with ethyl acetate three times, dried over magnesium sulfate and the solvent was removed to afford the crude product, which was taken to the next step without further purification. To a solution of allylic alchohol (520 mg, 2.5 mmol) in 7 ml MeOH was added dropwise 10% K_3CO_3 solution (3.3 mmol, 1.3 eq.). The reaction mixture was stirred at rt for 10 hrs until reaction completion indicated by TLC. The reaction was dilute with water, neutralized with 10% HCl solution, followed by extraction with ethyl acetate. The organic phase was washed with dilute hydrochloric acid, brined and dried over

magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 4:1 Hexane: Ethyl acetate).



Finally, *N*-protected carbamates were prepared according to literature procedure.[11] Sodium hydride was used as the base for deprotonation. To a solution of carbamate (430 mg, 2.5 mmol) in THF at 0 ^oC under argon was added NaH (5.0 mmol, 2.0 eq) in one portion and reaction was stirred for 1hr before TsCl (3.0 mmol, 1.2 eq) was added. The reaction was allowed to warm up to room temperature and kept stirring till reaction completion indicated by TLC (generally 1 hr). The reaction was quenched with sat. NH_4Cl solution after 0.5 hr, extracted with ethyl acetate. The organic phase was washed with brined, dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 5:1 Hexane: Ethyl acetate).



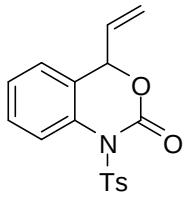
General procedure for catalytic decarboxylative dihydroquinoline synthesis from vinyl benzoxazinanones:

In a Schlenk tube under argon, $Pd(PPh_3)_4$ (0.05 mmol) and vinyl benzoxazinanone **1a** (1 mmol) were dissolved in 5 mL of methylene chloride. The resulting yellow solution was stirred at ambient temperature under Ar until the

completion of the reaction was indicated by TLC (generally 1h-4h). Following solvent evaporation under reduced pressure, the crude product was purified via flash chromatography (SiO_2, 7:1 Hexane: Ethyl acetate).

General procedure for catalytic decarboxylative dimer synthesis from vinyl benzoxazinanones:

In a Schlenk tube under argon, $Pd(PPh_3)_4$ (0.05 mmol) and vinyl benzoxazinanone **1** (1 mmol) were dissolved in 5 mL of toluene. The resulting yellow solution was stirred at ambient temperature under Ar until reaction completion was indicated by TLC (ca. 10 min). Following solvent evaporation under reduced pressure, the crude product was purified via flash chromatography (SiO_2, 2:1 Hexane: Ethyl acetate).

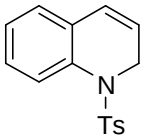


1-tosyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

32a (cw3124)

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (2H, d, *J*=8.3 Hz: Ar C*H*), 7.62 (1H, d, *J*=8.2 Hz: Ar C*H*), 7.40 (3H, m: Ar C*H*), 7.24 (3H, m: Ar C*H*), 6.04 (1H, ddd, *J*=17.0, 10.6, 6.1 Hz: =C*H*), 5.64 (1H, d, *J*=6.0 Hz: C*H*CH=), 5.46 (1H, dd, *J*=10.5, 0.6 Hz: CH=C*H*(*H*)$_Z$), 5.38 (1H, dd, *J*=17.2, 0.6 Hz: CH=C*H*(*H*)$_E$), 2.46 (3H, s: CH_3Ts).



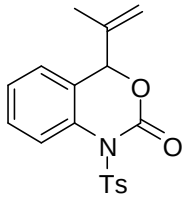
1-tosyl-1,2-dihydroquinoline
38a (cw3154)
White solid
$Pd(PPh_3)_4$: 65% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.67 (1H, d, *J*=8.08 Hz: Ar C*H*), 7.26 (2H, d, *J*=8.08 Hz: Ar C*H*), 7.23 (1H, dd, *J*=8.08, 1.77 Hz: Ar C*H*), 7.14 (1H, td, *J*=7.45, 1.26 Hz: Ar C*H*), 7.04 (2H, d, *J*=8.59 Hz: Ar C*H*), 6.90 (1H, dd, *J*=7.33, 1.52 Hz: Ar C*H*), 5.99 (1H, d, *J*=9.60 Hz: =C*H*), 5.55 (1H, dt, *J*=9.60, 4.17 Hz: =C*H*CH_2), 4.41 (2H, dd, *J*=4.17, 1.64 Hz: CH_2), 2.31 (3H, s: CH_3Ts).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.40 (quat. Ar *C*), 136.32 (quat. Ar *C*), 134.97 (quat. Ar *C*), 129.55 (quat. Ar *C*), 129.06 (Ar *C*H), 127.98 (Ar *C*H), 127.30 (Ar *C*H), 126.86 (Ar *C*H), 126.68 (Ar *C*H), 126.48 (Ar *C*H), 125.89 (=*C*H), 123.98 (=*C*HCH_2), 45.4 (*C*H_2), 21.6 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

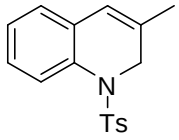
FTIR (CH_2Cl_2): ν_{max} 3053, 2986, 1421, 1262, 895

HRMS calcd for $C_{16}H_{15}NO_2SNa$ [M+Na] 308.0721, found 308.0729.



4-(prop-1-en-2-yl)-1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one
32a (cw3248)
White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.09 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.62 (1H, d, *J*=8.1 Hz: Ar C*H*), 7.39 (3H, m: Ar C*H*), 7.25 (1H, m: Ar C*H*), 7.15 (1H, m: Ar C*H*), 5.59 (1H, s: OC*H*), 5.17 (1H, s: =C*H*), 4.97 (1H, s: =C*H*), 2.46 (3H, s: CH_3Ts), 1.78 (3H, s: CH_3).



3-methyl-1-tosyl-1,2-dihydroquinoline

38b (cw3261)

White solid

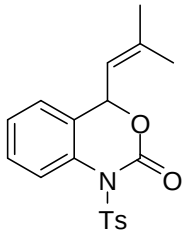
$Pd(PPh_3)_4$: 77% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (1H, d, *J*=7.83 Hz: Ar C*H*), 7.24 (2H, d, *J*=8.08 Hz: Ar C*H*), 7.19 (1H, dd, *J*=7.83, 1.52 Hz: Ar C*H*), 7.15 (1H, dd, *J*=7.45, 1.39 Hz: Ar C*H*), 7.05 (2H, d, *J*=8.34 Hz: Ar C*H*), 6.85 (1H, d, *J*=7.33 Hz: Ar C*H*), 5.71 (1 H, s: =C*H*), 4.24 (2 H, s: CH_2), 2.32 (3H, s: CH_3Ts), 1.64 (3H, s: CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.43 (quat. Ar *C*), 135.98 (quat. Ar *C*), 133.77 (quat. Ar *C*), 133.6 (=*C*), 130.6 (quat. Ar *C*), 128.9 (Ar *C*H), 126.9 (Ar *C*H), 126.9 (Ar *C*H), 126.8 (Ar *C*H), 125.7 (Ar *C*H), 120.9 (=*C*H), 49.4 (*C*H_2), 21.6 (*C*H_3Ts), 20.7 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3053, 2985, 1421, 1261, 895.

HRMS calcd for $C_{17}H_{17}NO_2SNa$ [M+Na] 322.0878, found 322.0879.

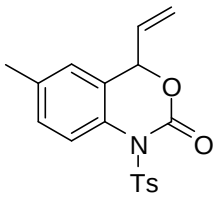


4-(2-methylprop-1-enyl)-1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

35a (cw3249)

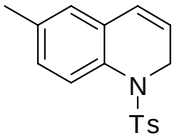
White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (1H, d, *J*=7.9 Hz: Ar C*H*), 7.28 (2H, m: Ar C*H*), 7.21 (2H, d, *J*=8.5 Hz: Ar C*H*), 7.07 (2H, d, *J*=8.0 Hz: Ar C*H*), 6.99 (1H, dd, *J*=7.4, 1.7 Hz: Ar C*H*), 5.98 (1H, d, *J*=9.3 Hz: OC*H*), 5.38 (1H, d, *J*=9.4 Hz: C*H*=),2.35 (3H, s: CH_3Ts), 1.46 (6H, s: CH_3).



6-methyl-1-tosyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one
cw3257
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.49 (1H, d, *J*=8.3 Hz: Ar C*H*), 7.37 (2H, d, *J*=8.7 Hz: Ar C*H*), 7.20 (1H, d, *J*=8.3 Hz: Ar C*H*), 6.97 (1H, s: Ar C*H*), 6.02 (1H, ddd, *J*=17.1, 10.5, 6.1 Hz: =C*H*), 5.58 (1H, d, *J*=6.1 Hz: C*H*CH=), 5.44 (1H, dd, *J*=10.4, 0.8 Hz: CH=C*H*(*H*)$_Z$), 5.35 (1H, d, *J*=17.2 Hz: CH=C*H*(*H*)$_E$), 2.45 (3H, s: overlapping C*H*$_3$Ts, C*H*$_3$), 2.35 (3H, s: overlapping C*H*$_3$Ts, C*H*$_3$).



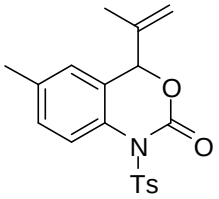
6-methyl-1-tosyl-1,2-dihydroquinoline
38c (cw3262)
White solid
$Pd(PPh_3)_4$: 50% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.59 (1 H, d, *J*=8.15 Hz: Ar C*H*), 7.31 (2 H, d, *J*=8.27 Hz: Ar C*H*), 7.08 (3 H, d, *J*=8.02 Hz: Ar C*H*), 6.75 (1 H, s: Ar C*H*), 5.98 (1 H, d, *J*=9.60 Hz: =C*H*), 5.56 (1 H, dt, *J*=9.60, 4.17 Hz: =C*H*CH$_2$), 4.41 (2 H, dd, *J*=4.04, 1.64 Hz: C*H*$_2$), 2.35 (3 H, s: overlapping C*H*$_3$Ts, C*H*$_3$), 2.32 (3 H, s: overlapping C*H*$_3$Ts, C*H*$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.26 (quat. Ar *C*), 136.46 (quat. Ar *C*), 136.39 (quat. Ar *C*), 132.41 (quat. Ar *C*), 129.31 (quat. Ar *C*), 129.03 (Ar *C*H), 128.67 (Ar *C*H), 127.34 (Ar *C*H), 126.99 (Ar *C*H), 126.71 (Ar *C*H), 125.95 (=*C*H), 123.84 (=*C*HCH$_2$), 45.46 (*C*H$_2$), 21.55 (overlapping *C*H$_3$, *C*H$_3$Ts), 21.03 (overlapping *C*H$_3$, *C*H$_3$Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3053, 2986, 1489, 1421, 1271, 1258, 895

HRMS calcd for $C_{17}H_{18}NO_2S$ [M+] 300.1058, found 300.1059.

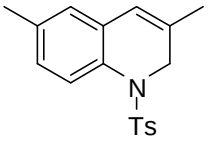


6-methyl-4-(prop-1-en-2-yl)-1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

35g (cw4204)

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (2H, d, *J*=8.3 Hz: Ar C*H*), 7.52 (1H, d, *J*=8.4 Hz: Ar C*H*), 7.39 (2H, d, *J*=8.0 Hz: Ar C*H*), 7.23 (1H, d, *J*=8.4 Hz: Ar C*H*), 6.97 (1H, s: Ar C*H*), 5.57 (1H, s: OC*H*), 5.18 (1H, s: =C*H*), 4.99 (1H, s: =C*H*), 2.48 (3H, s: overlapping CH_3Ts, CH_3), 2.38 (3H, s: overlapping CH_3Ts, CH_3), 1.80 (3H, s: CH_3C=).



3,6-dimethyl-1-tosyl-1,2-dihydroquinoline

38d (cw4207)

White solid

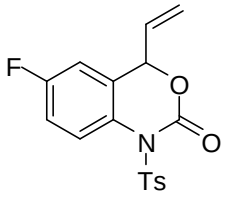
$Pd(PPh_3)_4$: 94% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.56 (1 H, d, *J*=8.15 Hz: Ar C*H*), 7.26 (2 H, d, *J*=8.21 Hz: Ar C*H*), 7.07 (2 H, d, *J*=8.27 Hz: Ar C*H*), 7.03 (1 H, dd, *J*=8.08, 1.52 Hz: Ar C*H*), 6.68 (1 H, s: Ar C*H*), 5.67 (1 H, s: =C*H*), 4.23 (2 H, s: CH_2), 2.35 (3 H, s: overlapping CH_3Ts, CH_3), 2.31 (3 H, s: overlapping CH_3Ts, CH_3), 1.63 (3 H, s: =CCH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.32 (quat. Ar *C*), 136.51 (quat. Ar *C*), 135.98 (quat. Ar *C*), 133.58 (=*C*), 131.02 (quat. Ar *C*), 130.34 (quat. Ar *C*), 128.96 (Ar *C*H), 127.67 (Ar *C*H), 126.88 (Ar *C*H), 126.64 (Ar *C*H), 126.22 (Ar *C*H), 121.00 (=*C*H), 49.48 (*C*H_2), 21.57 (overlapping *C*H_3Ts, *C*H_3), 21.08 (overlapping *C*H_3Ts, *C*H_3), 20.78 (=C*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

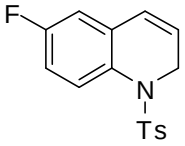
FTIR (CH_2Cl_2): ν_{max} 3054, 2926, 1493, 1346, 1271.

HRMS calcd for $C_{18}H_{23}N_2O2S$ [M+NH4] 331.1480, found 331.1479.



6-fluoro-1-tosyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one
cw3288
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.08 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.60 (1H, dd, *J*=9.1, 4.5 Hz: Ar C*H*), 7.39 (2H, dd, *J*=8.1, 0.6 Hz: Ar C*H*), 7.13 (1H, td, *J*=8.5, 2.9 Hz: Ar C*H*), 6.92 (1H, dd, *J*=7.7, 2.8 Hz: Ar C*H*), 6.01 (1H, ddd, *J*=17.0, 10.6, 6.2 Hz: =C*H*), 5.60 (1H, d, *J*=6.2 Hz: C*H*CH=), 5.50 (1H, d, *J*=10.4 Hz: CH=C*H*(H)$_Z$), 5.40 (1H, d, *J*=17.6 Hz: CH=C*H*(H)$_E$), 2.47 (3H, s: CH_3Ts).



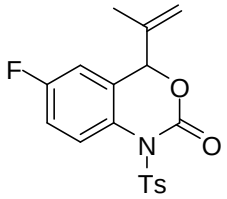
6-fluoro-1-tosyl-1,2-dihydroquinoline
38e (cw3298)
White solid
$Pd(PPh_3)_4$: 51% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (1 H, dd, *J*=8.72, 5.05 Hz: Ar C*H*), 7.28 (2 H, d, *J*=8.34 Hz: Ar C*H*), 7.08 (2 H, d, *J*=8.46 Hz: Ar C*H*), 6.96 (1 H, td, *J*=8.57, 2.94 Hz: Ar C*H*), 6.63 (1 H, dd, *J*=8.59, 2.91 Hz: Ar C*H*), 5.95 (1 H, d, *J*=9.66 Hz: =C*H*), 5.63 (1 H, dt, *J*=9.19, 4.20 Hz: =C*H*CH_2), 4.42 (2 H, dd, *J*=4.11, 1.71 Hz: CH_2), 2.35 (3 H, s: CH_3Ts).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.6 quat. Ar *C*), 136.0 (quat. Ar *C*), 129.1 (Ar *C*H), 128.9 (quat. Ar *C*), 128.8 (quat. Ar *C*), 127.8 (quat. Ar *C*), 127.3 (Ar *C*H), 125.5 (=*C*HCH_2), 125.2 (=*C*H), 114.4 Ar *C*H), 112.9 (Ar *C*H), 112.7 (Ar *C*H), 45.4 (*C*H_2), 21.5 (*C*H_3Ts).

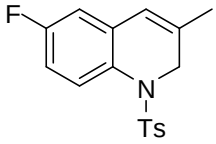
FTIR (CH_2Cl_2): ν_{max} 3063, 2926, 1713, 1487, 1352, 1167.

HRMS calcd for $C_{16}H_{18}FN_2O_2S$ [M+NH_4] 321.1073, found 321.1074.



6-fluoro-4-(prop-1-en-2-yl)-1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one
cw3289
colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (2H, d, *J*=8.3 Hz: Ar C*H*), 7.60 (1H, dd, *J*=9.0, 4.5 Hz: Ar C*H*), 7.38 (2H, d, *J*=8.0 Hz: Ar C*H*), 7.12 (1H, td, *J*=8.2, 2.5 Hz: Ar C*H*), 6.88 (1H, dd, *J*=7.7, 2.8 Hz: Ar C*H*), 5.56 (1H, s: OC*H*), 5.20 (1H, s: =C*H*), 4.99 (1H, s: =C*H*), 2.47 (3H, s: CH_3Ts), 1.78 (3H, s: CH_3).



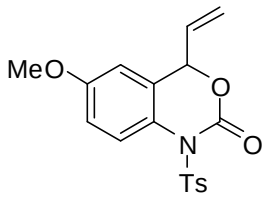
6-fluoro-3-methyl-1-tosyl-1,2-dihydroquinoline
38f (cw3293)
White solid
$Pd(PPh_3)_4$: 82% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.64 (1 H, dd, *J*=8.81, 5.21 Hz: Ar C*H*), 7.25 (2 H, d, *J*=8.34 Hz: Ar C*H*), 7.09 (2 H, d, *J*=8.46 Hz: Ar C*H*), 6.91 (1 H, td, *J*=8.59, 2.91 Hz: Ar C*H*), 6.56 (1 H, dd, *J*=8.75, 2.87 Hz: Ar C*H*), 5.66 (1 H, s: =C*H*), 4.25 (2 H, s: CH_2), 2.35 (3 H, s: CH_3Ts), 1.66 (3 H, s: CH_3).
.

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.01 (quat. Ar *C*), 143.63 (quat. Ar *C*), 135.69 (quat. Ar *C*), 135.53 (quat. Ar *C*), 132.40 (=*C*), 129.35 (quat. Ar *C*), 129.05 (Ar *C*H), 128.56 (Ar *C*H), 126.86 (Ar *C*H), 120.36 (=*C*H), 113.39 (Ar *C*H), 111.83 (Ar *C*H), 49.46 (*C*H_2), 21.54 (*C*H_3Ts), 20.72 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3053, 2986, 1480, 1348, 1166.

HRMS calcd for $C_{17}H_{16}FNO_2S$ [M+] 317.0886, found 317.0887.

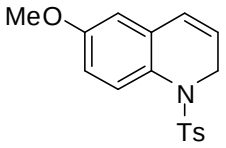


6-methoxy-1-tosyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

cw4142

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.06 (2H, d, *J*=8.5 Hz: Ar C*H*), 7.52 (1H, d, *J*=9.0 Hz: Ar C*H*), 7.37 (2H, d, *J*=8.5 Hz: Ar C*H*), 6.93 (1H, dd, *J*=9.0, 2.8 Hz: Ar C*H*), 6.69 (1H, d, *J*=2.8 Hz: Ar C*H*), 6.01 (1H, ddd, *J*=17.0, 10.6, 6.1 Hz: =C*H*), 5.58 (1H, d, *J*=6.0 Hz: C*H*CH=), 5.45 (1H, d, *J*=11.1 Hz: CH=C*H*$(H)_Z$), 5.37 (1H, d, *J*=17.2 Hz: CH=C*H*$(H)_E$), 3.81 (3H, s: OCH_3), 2.46 (3H, s: CH_3Ts).



6-methoxy-1-tosyl-1,2-dihydroquinoline

38g (cw4194)

White solid

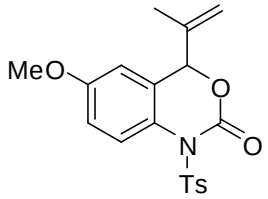
$Pd(PPh_3)_4$: 80% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.62 (1 H, d, *J*=8.84 Hz: Ar C*H*), 7.28 (2 H, d, *J*=8.34 Hz: Ar C*H*), 7.09 (1 H, d, *J*=8.53 Hz: Ar C*H*), 6.82 (1 H, dd, *J*=8.81, 2.94 Hz: Ar C*H*), 6.47 (1 H, d, *J*=2.91 Hz: Ar C*H*), 5.95 (1 H, d, *J*=9.60 Hz: =C*H*), 5.56 (1 H, dt, *J*=9.60, 4.04 Hz: =C*H*CH_2), 4.40 (2 H, dd, *J*=4.07, 1.67 Hz: CH_2), 3.81 (3 H, s: OCH_3), 2.35 (3 H, s: CH_3Ts).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.20 (quat. Ar *C*), 143.30 (quat. Ar *C*), 136.14 (quat. Ar *C*), 130.69 (quat. Ar *C*), 129.03 (Ar *C*H), 128.35 (Ar *C*H), 127.78 (quat. Ar *C*), 127.39 (Ar *C*H), 125.84 (=*C*), 124.60 (=*C*HCH_2), 113.02 (Ar *C*H), 111.53 (Ar *C*H), 55.48 (O*C*H_3), 45.54 (*C*H_2), 21.57 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3050, 2923, 1491, 1350, 1271.

HRMS calcd for $C_{17}H_{17}NO_3SNa$ [M+Na] 338.0827, found 338.0828.



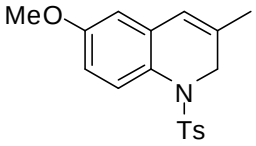
6-methoxy-4-(prop-1-en-2-yl)-1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

cw4196

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.08 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.55 (1H, d, *J*=9.0 Hz: Ar C*H*), 7.39 (2H, d, *J*=8.5 Hz: Ar C*H*), 6.95 (1H, dd, *J*=9.0, 2.8 Hz: Ar C*H*), 6.69 (1H, d, *J*=2.7 Hz: Ar C*H*), 5.55 (1H, s: OC*H*), 5.17 (1H, s: =C*H*), 4.99 (1H, s: =C*H*), 3.83 (3H, s: OCH_3), 2.48 (3H, s: CH_3Ts), 1.79 (3H, s: CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.4 (*C*ONTS), 149.4 (quat. Ar *C*), 145.5 (=*C*), 139.5 (quat. Ar *C*), 135.8 (quat. Ar *C*), 129.6 (Ar *C*H), 129.0 (Ar *C*H), 127.6 (quat. Ar *C*), 127.2 (quat. Ar *C*), 122.2 (Ar *C*H), 117.2 (Ar *C*H), 114.0 (Ar *C*H), 111.2 (=*C*H), 82.2 (O*C*H), 55.7 (O*C*H_3), 21.7 (*C*H_3Ts), 18.4 (*C*H_3).



6-methoxy-3-methyl-1-tosyl-1,2-dihydroquinoline

38h (cw4200)

White solid

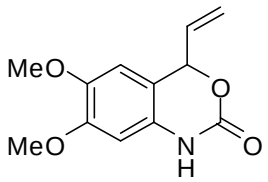
$Pd(PPh_3)_4$: 92% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61 (1 H, d, *J*=8.78 Hz: Ar C*H*), 7.25 (2 H, d, *J*=8.27 Hz: Ar C*H*), 7.09 (2 H, d, *J*=8.08 Hz: Ar C*H*), 6.79 (1 H, dd, *J*=8.78, 2.91 Hz: Ar C*H*), 6.41 (1 H, d, *J*=2.84 Hz: Ar C*H*), 5.66 (1 H, s: =C*H*), 4.23 (2 H, s: CH_2), 3.81 (3 H, s: OCH_3), 2.36 (3 H, s: CH_3Ts), 1.65 (3 H, s: CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.28 (quat. Ar *C*), 143.34 (quat. Ar *C*), 135.77 (quat. Ar *C*), 134.41 (=*C*), 131.76 (quat. Ar *C*), 128.94 (Ar *C*H), 128.16 (Ar *C*H), 126.91 (Ar *C*H), 126.46 (quat. Ar *C*), 120.97 (=*C*H), 111.97 (Ar *C*H), 110.77 (Ar *C*H), 55.45 (O*C*H_3), 49.58 (*C*H_2), 21.57 (*C*H_3Ts), 20.78 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3052, 2929, 1346, 1259, 1165

HRMS calcd for $C_{18}H_{19}NO_3SNa$ [M+Na] 352.0984, found 352.0982.

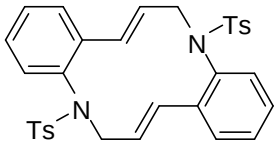


6,7-dimethoxy-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

36a (cw4060)

White solid

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.48 (1H, br. s.: N*H*), 6.60 (1H, s: Ar C*H*), 6.35 (1H, s: Ar C*H*), 6.05 (1H, ddd, *J*=17.0, 10.4, 6.5 Hz: =C*H*), 5.74 (1H, d, *J*=6.6 Hz: C*H*CH=), 5.41 (1H, d, *J*=10.4 Hz: CH=C*H*$(H)_Z$), 5.36 (1H, d, *J*=17.4 Hz: CH=C*H*$(H)_E$), 3.87 (3H, s: OCH_3), 3.84 (3H, s: OCH_3).



(7E,15E)-5,13-ditosyl-5,6,13,14-tetrahydrodibenzo[b,h][1,7]diazacyclododecine

39a (cw4017)

White solid

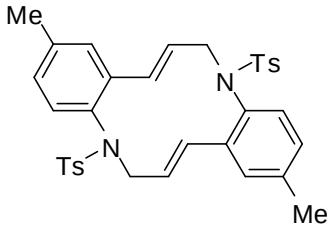
$Pd(PPh_3)_4$: 36% yield, dr = 8:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (4 H, d, *J*=8.1 Hz: Ar C*H*), 7.50 (2 H, d, *J*=16.4 Hz: =C*H*), 7.41 (4 H, d, *J*=8.6 Hz: Ar C*H*), 7.28 (2 H, d, *J*=8.7 Hz: Ar C*H*), 7.15-7.25 (4 H, m: Ar C*H*), 6.94 (2 H, d, *J*=7.8 Hz: Ar C*H*), 5.46 (2 H, dt, *J*=16.1, 5.9 Hz: =C*H*CH_2), 4.66 (2 H, ddd, *J*=13.2, 5.9, 1.3 Hz: CH_2), 3.73 (6 H, s: CH_3), 3.62 (2 H, dd, *J*=13.2, 5.9 Hz: CH_2), 2.47 (6 H, s: CH_3Ts).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.9 (quat. Ar *C*), 139.0 (quat. Ar *C*), 137.3 (=*C*H), 136.0 (quat. Ar *C*), 130.0 (Ar *C*H), 129.6 (quat. Ar *C*), 129.0 (Ar *C*H), 128.5 (Ar *C*H), 128.4 (Ar *C*H), 128.2 (Ar *C*H), 127.0 (Ar *C*H), 124.6 (=*C*HCH_2), 50.9 (*C*H_2), 21.7 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 30513, 2926, 1346, 1271, 1161, 760.

HRMS calcd for $C_{32}H_{34}N_3O_4S_2$ [M+NH_4] 588.1991, found 588.1990.



(7*E*,15*E*)-2,10-dimethyl-5,13-ditosyl-5,6,13,14-tetrahydrodibenzo[*b*,*h*][1,7]diazacyclododecine

39b (cw4223)

White solid

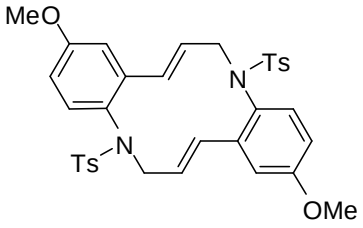
$Pd(PPh_3)_4$: 87% yield, dr =5.5:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (4H, d, *J*=8.2 Hz: Ar C*H*), 7.42 (6H, m: overlapping Ar C*H*, =C*H*), 7.07 (1H, s: Ar C*H*), 6.97 (2H, d, *J*=8.3 Hz: Ar C*H*), 6.81 (2H, d, *J*=8.1 Hz: Ar C*H*), 5.44 (2H, dt, *J*=16.2, 6.0 Hz: =C*H*CH_2), 4.63 (2H, ddd, *J*=13.1, 6.0, 1.5 Hz: C*H*$_2$), 3.63 (2H, dd, *J*=13.1, 5.9 Hz: C*H*$_2$), 2.48 (6 H, s: C*H*$_3$Ts), 2.25 (6 H, s: C*H*$_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 138.8 (quat. Ar *C*), 143.8 (quat. Ar *C*), 138.6 (quat. Ar *C*), 137.4 (=*C*H), 136.1 (quat. Ar *C*), 134.7 (quat. Ar *C*), 129.9 (Ar *C*H), 129.3 (Ar *C*H), 128.2 (Ar *C*H), 128.1 (Ar *C*H), 127.6 (Ar *C*H), 124.3 (=*C*HCH_2), 50.8 (*C*H_2), 21.7 (*C*H_3Ts), 21.2 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 2924, 1599, 1491, 1346, 1163.

HRMS calcd for $C_{34}H_{38}N_3O_4S_2$ [NH_4] 616.2304, found 616.2302.



(7*E*,15*E*)-2,10-dimethoxy-5,13-ditosyl-5,6,13,14-tetrahydrodibenzo[*b*,*h*][1,7]diazacyclododecine

39c (cw4205)

White solid

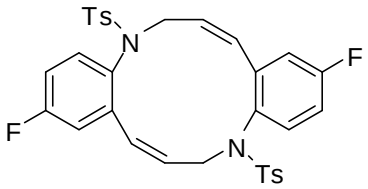
$Pd(PPh_3)_4$: 94% yield, dr = 6.7:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (4 H, d, *J*=8.21 Hz: Ar C*H*), 7.35 - 7.54 (6 H, m: overlapping Ar C*H*, =C*H*), 6.82 (2 H, d, *J*=8.72 Hz: Ar C*H*), 6.76 (2 H, d, *J*=2.91 Hz: Ar C*H*), 6.69 (2 H, dd, *J*=8.72, 2.84 Hz: Ar C*H*), 5.46 (2 H, dt, *J*=16.14, 5.89 Hz: =C*H*CH_2), 4.66 (2 H, ddd, *J*=13.17, 5.87, 1.29 Hz: C*H*$_2$), 3.73 (6 H, s: C*H*$_3$), 3.62 (2 H, dd, *J*=13.17, 5.91 Hz: C*H*$_2$), 2.47 (6 H, s: C*H*$_3$Ts).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.5 (quat. Ar *C*), 143.8 quat. Ar *C*), 140.1 (quat. Ar *C*), 137.2 (=*C*H), 136.1 (quat. Ar *C*), 129.9 (Ar *C*H), 129.4 (Ar *C*H), 128.1 (Ar *C*H), 124.9 (=*C*HCH$_2$), 114.1 (Ar *C*H), 111.7 (Ar *C*H), 55.4 (O*C*H$_3$), 50.8 (*C*H$_2$), 21.7 (*C*H$_3$Ts); Note: one quat. Ar carbon is not found. The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3065, 2926, 1599, 1570, 1493, 1258, 1161.

HRMS calcd for $C_{34}H_{34}N_2O_6S_2Na$ [M+Na] 653.1756, found 653.1762.



(7*Z*,15*Z*)-2,10-difluoro-5,13-ditosyl-5,6,13,14-tetrahydrodibenzo[*b*,*h*][1,7]diazacyclododecine

39d (cw4210)

Colorless oil

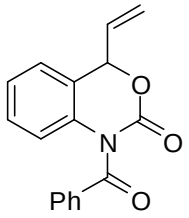
$Pd(PPh_3)_4$: 92% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.53 (2 H, d, *J*=8.15 Hz: Ar C*H*), 7.33 (4 H, d, *J*=8.21 Hz: Ar C*H*), 7.19 - 7.26 (2 H, m: Ar C*H*), 7.11 (4 H, d, *J*=7.89 Hz: Ar C*H*), 6.91 (2 H, t, *J*=8.75 Hz: Ar C*H*), 6.29 (2 H, d, *J*=9.73 Hz: =C*H*), 5.67 (2 H, dt, *J*=9.79, 4.26 Hz: =C*H*CH$_2$), 4.46 (4 H, dd, *J*=3.73, 1.39 Hz: C*H*$_2$), 2.36 (6 H, s: C*H*$_3$Ts),

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.80 (quat. Ar *C*), 156.82 (quat. Ar *C*), 143.78 (quat. Ar *C*), 136.15 (quat. Ar *C*), 129.25 (Ar *C*H), 128.20 (Ar *C*H), 127.23 (Ar *C*H), 124.33 (=C*H*), 122.33 (Ar *C*H), 118.55 (=C*H*CH$_2$), 117.84 (quat. Ar *C*), 113.03 (Ar *C*H), 45.14 (*C*H$_2$), 21.59 (*C*H$_3$Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR (CH_2Cl_2): ν_{max} 3065, 2926, 1612, 1472, 1263, 1167, 750.

HRMS calcd for $C_{32}H_{28}F_2N_2O_4S_2Na$ [M+Na] 629.1356, found 629.1359.

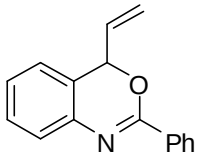


1-benzoyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

37e (cw3159)

Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (2H, d, *J*=8.1 Hz: Ar C*H*), 7.62 (1H, t, *J*=7.5 Hz: Ar C*H*), 7.55 (1H, d, *J*=8.1 Hz: Ar C*H*), 7.49 (2H, t, *J*=7.8 Hz: Ar C*H*), 7.36 (1H, m: Ar C*H*), 7.26 (2H, d, *J*=15.2 Hz: Ar C*H*), 6.27 (1H, td, *J*=11.2, 5.2 Hz: =C*H*), 5.93 (1H, d, *J*=5.6 Hz: C*H*CH=),5.59 (1H, dd, *J*=10.4, 0.6 Hz: CH=C*H*(*H*)$_Z$), 5.46 (6 H, d, *J*=17.2 Hz: CH=C*H*(*H*)$_E$)).



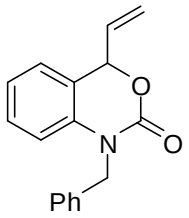
2-phenyl-4-vinyl-4*H*-benzo[*d*][1,3]oxazine

42f (cw3164)

White solid

$Pd(PPh_3)_4$: 96% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.17 (2H, dd, *J*=8.3, 1.4 Hz: Ar C*H*), 7.68 (4H,m: Ar C*H*), 7.33 (3H, m: Ar C*H*), 6.11 (1H, m: =C*H*), 5.88 (1H, d, *J*=6.3 Hz: OC*H*), 5.33 (2H, m: =CH_2).



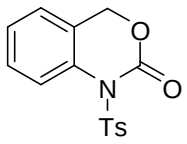
1-benzyl-4-vinyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

37a (cw3191)

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.37 (5H, m: Ar C*H*), 7.28 (1H, dd, *J*=15.6, 1.7 Hz: Ar C*H*), 7.19 (1H, d, *J*=6.4 Hz: Ar C*H*), 7.14 (1H, d, *J*=7.4 Hz: Ar C*H*), 6.92 (1H, d, *J*=8.2 Hz: Ar C*H*), 6.18 (1H, ddd, *J*=17.1, 10.4, 5.9 Hz: =C*H*), 5.85 (1H, d, *J*=6.0

Hz: C*H*CH=), 5.51 (1H, d, *J*=10.4 Hz: CH=C*H*$(H)_Z$), 5.42 (1H, d, *J*=17.1 Hz: CH=C*H*$(H)_E$), 5.24 (2H, m: CH_2Ph).



1-tosyl-1*H*-benzo[*d*][1,3]oxazin-2(4*H*)-one

cw4161

colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.14 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.60 (1H, d, *J*=8.4 Hz: Ar C*H*), 7.40 (3H, d, *J*=8.1 Hz: Ar C*H*), 7.24 (2H, d, *J*=6.4 Hz: Ar C*H*), 5.13 (2H, s: CH_2), 2.47 (3H, s: CH_3Ts).

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Chapter 3

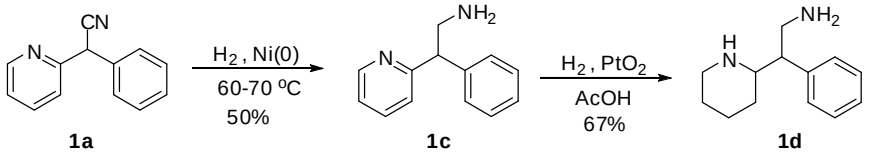
Palladium-catalyzed Decarboxylative Cycloaddition Reactions

3.1 Introduction

Substituted piperidines are frequently encountered structural motifs of alkaloids that are abundant in nature and have attracted much attention due to their significant biological activities.[1, 2] Statistics indicate that more that 12,000 piperidine derivatives have been claimed to be in clinical or preclinical studies.[3]

The industrial preparation of piperidines has largely relied on nickel-catalyzed hydrogenation of pyridine. The routine synthesis of piperdine in the laboratory is also achieved with resort to the reduction of the corresponding pyridines. For example, sodium in alcohol solvent has been employed to reduce pyridines. Transition metal-catalyzed hydrogenation is also used due to the mild reaction conditions and functional group compatibility. For instance, piperdine **1d** was prepared by selective reduction by resorting to different transition metals as shown in Scheme 1.[4]

Scheme 1 *Piperidines synthesis via transition metal-catalyzed reduction of pyridines*

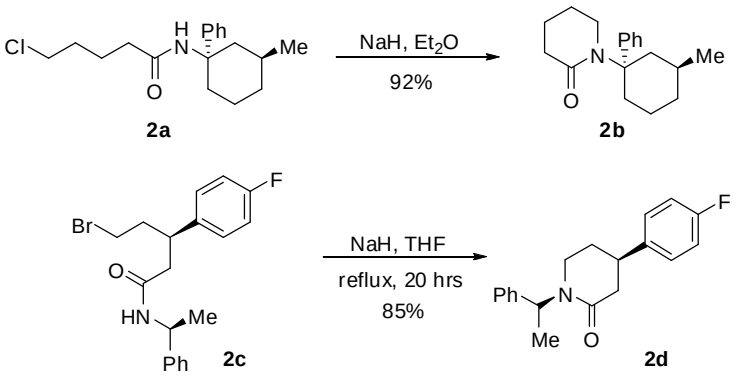


1a **1c** **1d**

Intramolecular *N*-cyclizations have also been widely used for piperidine ring preparation from precursors such as 1,5-amino halides, 1,5-diamino alcohols, 1,5-diamines and 1,5-dihalides.[5] For example, piperidines **2b** and **2d** were synthesized from the corresponding 1,5-aminohalides in good yields (Scheme 2).[6, 7]

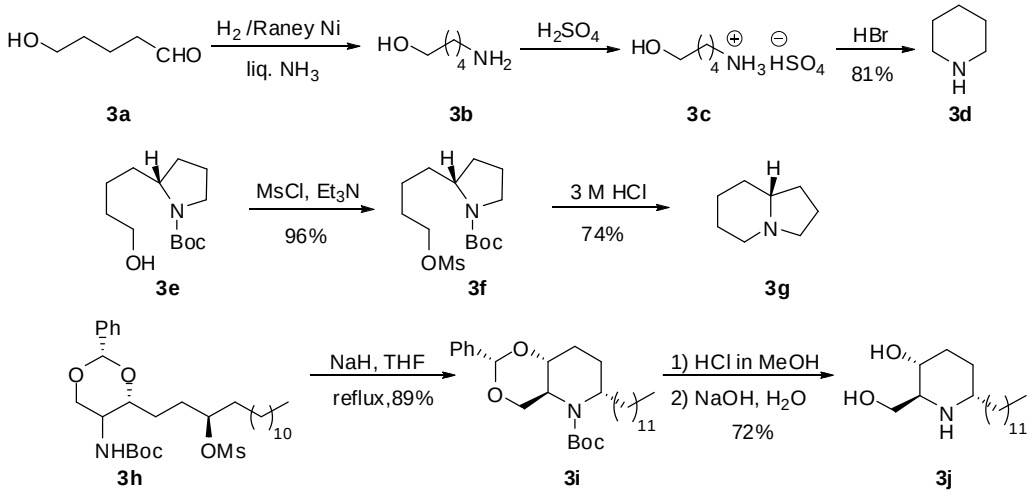
However, secondary amines with an electron withdrawing group were used to avoid competing side reactions such as dialkylation and intermolecular *N*-alkylation.

Scheme 2 *Piperidine synthesized from 1,5-aminohalides*



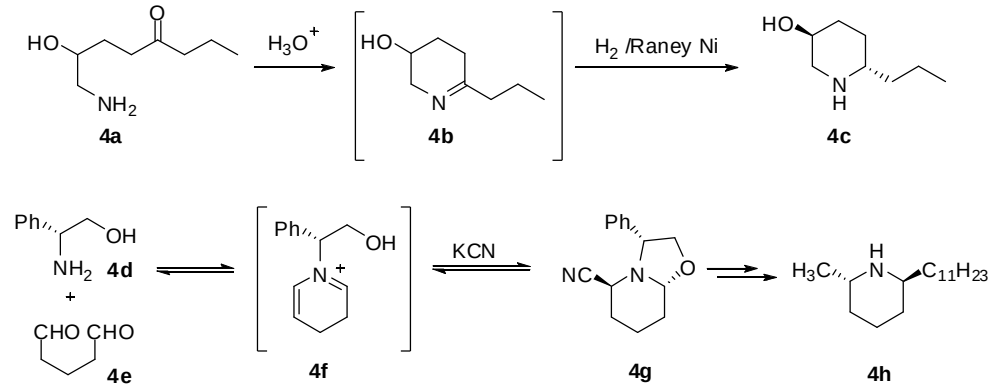
Intramolecular ring closure of 1,5-amino alcohols is another classical way for piperidine preparation (Scheme 3). In the late 1940's, Woods reported the synthesis of piperidine **3d** from a free 1,5-amino alcohol **3b**.[8] Conversion of **3b** to its sulfate salt **3c** was achieved by treatment with sulfuric acid and piperidine **3d** was formed by refluxing with hydrobromide acid. Similarly, piperidines **3g** and **3j** were prepared from their corresponding 1,5-aminoalcohols.[9, 10]

Scheme 3 *Piperidine synthesized from 1,5-aminoalcohols*



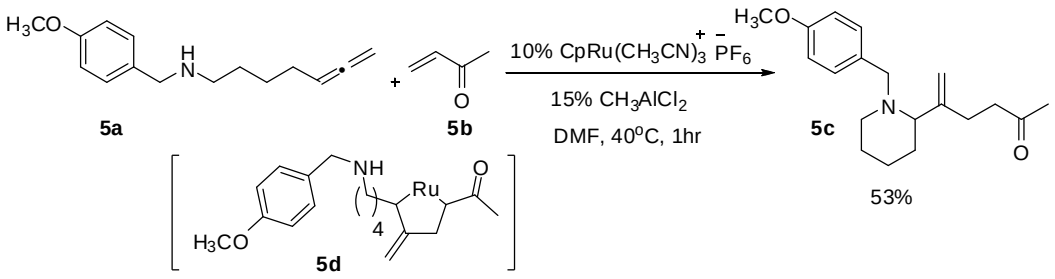
Pseudoconhydrine **4c** isolated along with coniine from Poison Hemlock, *conium maculatum* was synthesized via an intramolecular reductive amination of intermediate **4b** (Scheme 4).[9] Alkaloid solenopsine **4h**, a subcategory of ant venoms, displays potent antifungal, insecticide and repellent activity.[14,15] The synthesis featured a intermolecular double condensations of (-)-phenylglycinol **4d** and glutaraldehyde **4e** to form an iminium intermediate **4f**, which was trapped by KCN to furnish cyanopiperidine **4g**. Further elaborations provided the alkaloid product **4h**.[10]

Scheme 4 *Piperidines synthesis via an imine intermediate*



Transition metal-mediated piperidine synthesis has drawn a lot of attention. In 2000, Trost reported a ruthenium-catalyzed piperidine synthesis from allene **5a** and enone **5b** (Scheme 5).[11] A ruthenacycle **5d** was thought to be involved, and subsequent intramolecular nucleophilic attack to furnish the piperdine product **5c** in 53% yield.

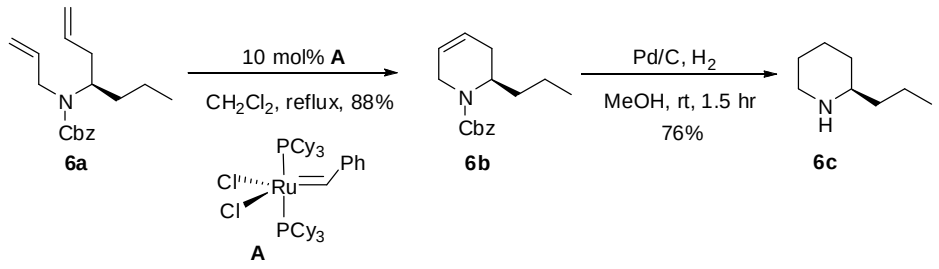
Scheme 5 *Piperidines synthesis via a ruthenacycle*



Ring closing methathesis (RCM) has also been applied in piperidine synthesis as shown in Scheme 6.[14] Tetrahydropyridine **6b** was prepared by treatment of compound **6a** with 10 mol% Grubbs' catalyst **A**, and (*R*)-coniine **6c** was obtained upon further

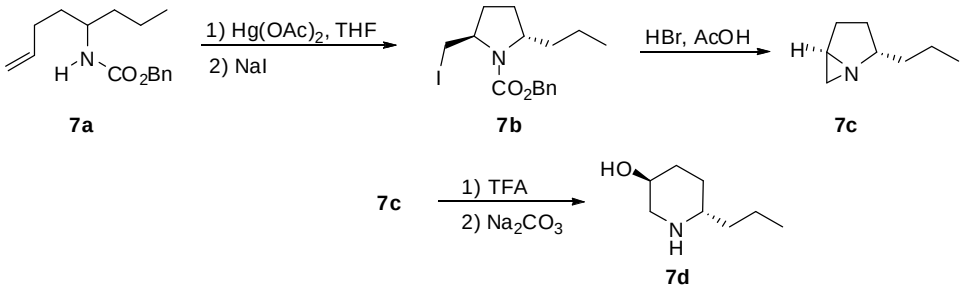
elaboration. Coniine **6c** is a poisonous alkaloid, which is found in poison hemlock and the yellow pitcher plant.[12]

Scheme 6 *Piperidines synthesis via Ring closing methathesis (RCM)*



An intramolecular aminomercuration protocol was developed by Harding and applied in the synthesis of alkaloid (±)-Pseudoconhydrine **7d** (Scheme 7).[13, 14] Aziridine **7c** was formed from iodo compound **7b** upon treatment of hydrobromide in acetic acid. Electrophilic ring opening followed by hydrolysis yield the alkaloid product **7d** in 50% yield.

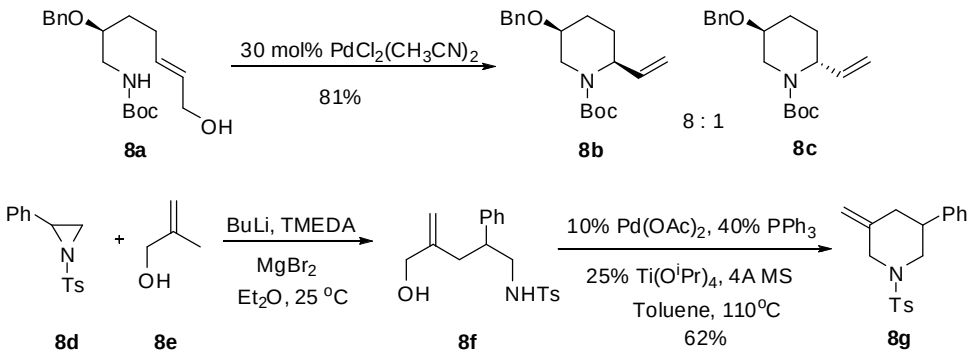
Scheme 7 *Piperidines synthesis via intramolecular aminomercuration*



Palladium catalysts have also been used for the synthesis of piperidine alkaloids (Scheme 8). For example, Hirai reported an efficient Pd-catalyzed intramolecular

N-alkylation to yield a mixture of diastereoisomers **8b** and **8c** in a ratio of 8:1.[15] In 2005, Harrity reported a stepwise [3+3] cycloaddtion for constructing the piperidine ring system.[16] Aziridine **8d** was allowed to react with allylic alcohol **8e** under strong basic conditions to yield the corresponding amine product **8f**, which, upon intramolecular cyclization generated piperdine alkaloid **8g** in the presence of $Pd(OAc)_2$ and a cocatalytic $Ti(O^iPr)_4$. A Pd π-allyl intermediate was generated during the course of this reaction, and ring closure of carbamates with free allylic alcohols has been catalyzed by Pd(II) catalysts.[17]

Scheme 8 *Piperidines synthesis from Pd-catalyzed intramolecular N-annulations*

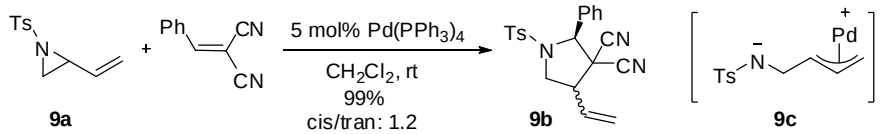


Even though there are many synthetic methods for piperdine ring preparation, the substrates availability, harsh reaction conditions and functional group tolerance are some limitations of the current methods. Therefore, the need for a novel and efficient method for substituted piperidine synthesis, especially highly-substituted piperidines still exists.

3.2 Synthesis of Highly-substituted Piperidines

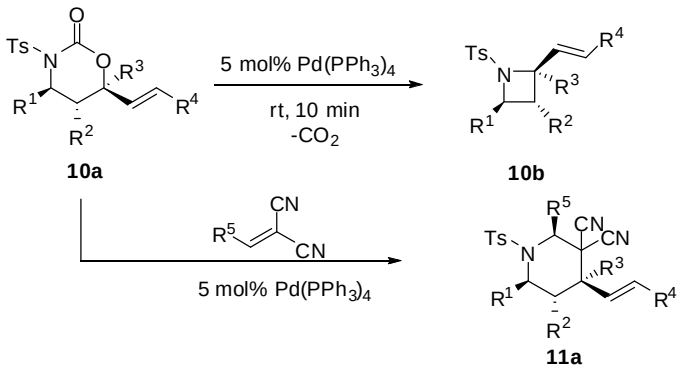
In 2002, Yamamoto reported an efficient synthesis of pyrrolidine derivative **9b** via Pd-catalyzed ring expansion of vinyl azetidine **9a** in the presence of electron-poor olefin; however, the pyrrolidine product was formed in very low diastereoselectivity (dr = 1.2). The reaction was thought to proceed by forming a zwitterionic π-allyl palladium intermediate **9c** from vinyl azetidine in the presence of Pd catalyst.[18]

Scheme 9 *Nitrogen nucleophiles in Pd-catalyzed allylation reactions*



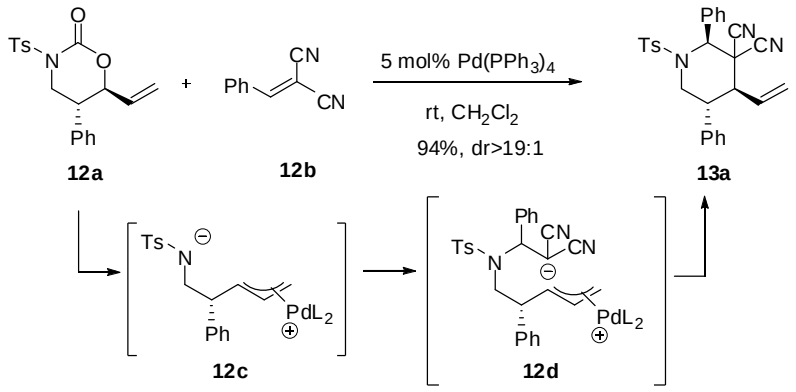
We have previously shown that vinyl oxazinanones **10a** underwent catalytic diastereoselective decarboxylative ring contraction to form vinyl azetidines **10b** under mild conditions in good yield (Scheme 11).[19] In addition to the decarboxylative ring contractions, it was envisioned that performing the decarboxylation in the presence of Michael acceptors would result in decarboxylative olefin insertion to provide highly-substituted vinyl piperidines **11a**.

Scheme 10 *Decarboxylative olefin insertion reactions with vinyl oxazinanones*



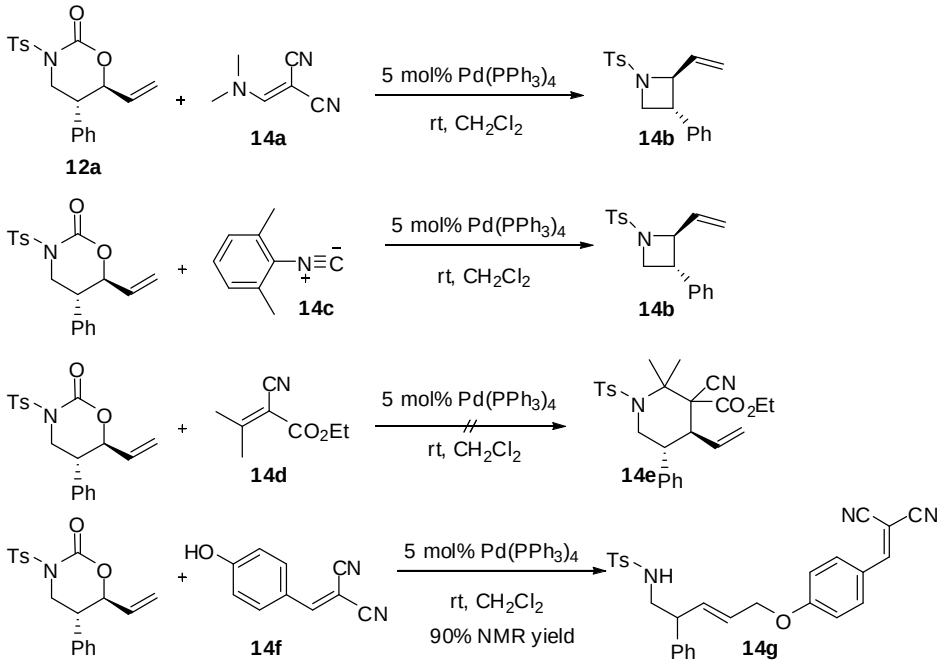
Upon Pd-facilitated decarboxylation, zwitterionic π-allyl intermediates **12c** should lend themselves to decarboxylative olefin insertion if the intermediate amide anion could be intercepted by a suitably electrophilic Michael acceptor (Scheme 11).[21-23] The resulting stabilized carbanion **12d** could undergo addition to the π-allyl palladium fragment which would give rise to 4-vinyl piperidines. Indeed, treatment of *rac*-**12a** with benzylidenemalononitrile and $Pd(PPh_3)_4$ produced the vinyl piperidine **13a** as a single diastereoisomer in excellent yield. The reaction is rapid, and vinyl azetidines are not observed as intermediates when the reaction is monitored by ^1H NMR spectroscopy. Once again, *cis*-**12a** provides the same product as *trans*-**12a**, indicating that π-allyl epimerization is faster than cyclization.

Scheme 11 *Decarboxylative olefin insertion reactions with vinyl oxazinanones*



Other Michael acceptors were also tried with our standard reaction conditions as shown in Scheme 12. It turned out that the electronics of the Michael acceptors are crucial to the success of the decarboxylative cycloaddition reactions. The same phenomenon has been observed in the Ru-catalyzed tandem Michael addition-allylation reactions.[20] Not surprisingly, when Michael acceptor such as **14a** or dipolarphile **14c** was employed, no cycloaddition product was observed and the decarboxylative ring contraction product was formed exclusively. In the case of ethyl cyanobutenoate **14d**, azetidine **14b** was generated first and later transformed to a messy polymeric mixture. Of note here is that when *p*-hydroxybenzylidene malononitrile was employed as the electrophile, the *O*-allylation product **14g** was formed exclusively in 90% NMR yield, which in turn supported that a zwitterionic π-allyl intermediate was formed first then subsequently quenched by the nucleophile present.

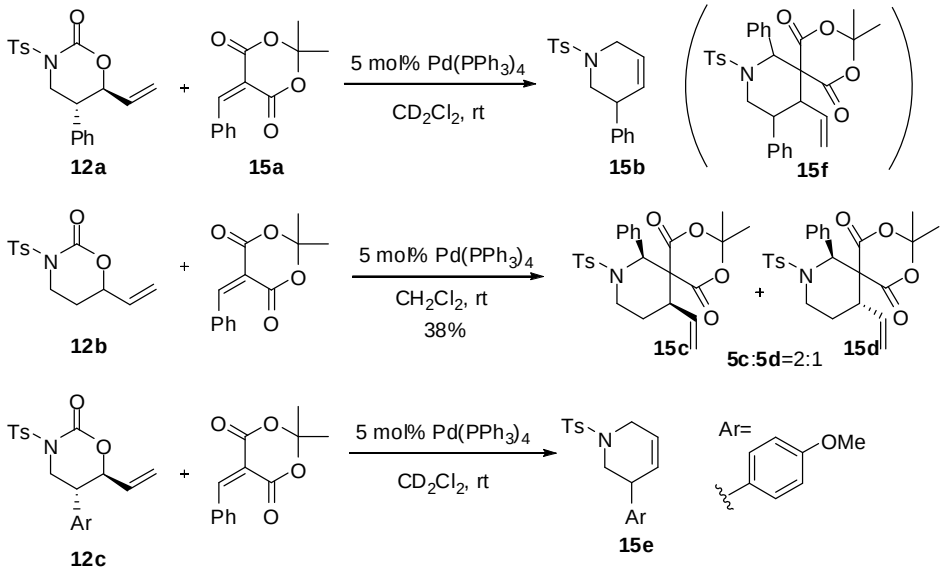
Scheme 12 *Problematic Michael acceptors*



Interesting chemoselectivity was observed when a sterically-hindered Michael acceptor **15a** was used (Scheme 13). Treatment of vinyl oxazinanone **12a** with 5 mol% $Pd(PPh_3)_4$ in the presence of **15a** at rt yielded the unexpected tetrahydropyridine ring product **15b** exclusively in 10 mins. Interestingly, the scale-up reaction gave a 1:1 mixture of products **15b** and cycloaddition adduct **15f** in 99% combined yield. This chemoselectivity was interesting since it has been shown that, in the absence of benzylidenemalononitrile, the four-membered vinyl azetidine product is favored over the tetrahydropyridine due to stereoelectronic effects. We reasoned that cycloaddition could be favored if the substrate was less sterically demanding so the unsubstituted vinyl oxazinanone **12b** was prepared in that regard. Treatment of

12b under our standard reaction conditions produced the six-membered cycloaddition product in 38% isolated yield with no observation of piperidine product. The lower yield was attributed to the formation of a polymer-type byproduct, which has been observed when the decarboxylative ring contraction was performed with vinyl oxazinanone **12b** in the absence of Michael acceptor. As expected, this chemoselectivity was switched back when vinyl oxazinanone **12c** was used, and the six-membered ring product **15e** was generated exclusively in 80% NMR yield.

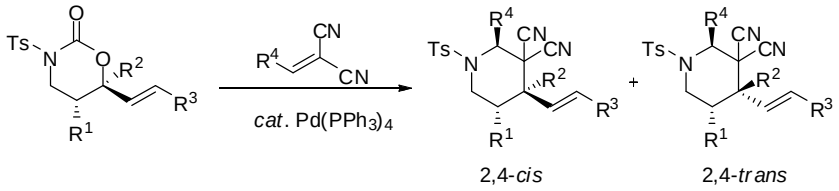
Scheme 13 *Interesting chemoselectivity*



Ultimately, if the Michael acceptors are properly chosen, a variety of vinyl oxazinanones undergo smooth decarboxylative cycloaddition reactions (Table 1). Although the stereocontrol is good when the vinyl oxazinanone is substituted at C_4, C_5, or C_6, the stereocontrol is not high when the vinyl oxazinanone is unsubstituted

(i.e., **13j**,**k** *trans*/*cis*~3:1, Table 1) or with a small substituent (i.e., **13l**,**m** *trans*/*cis*=2:1, Table 1).

Table 1 *Yields and diastereoselectivities of decarboxylative olefin insertions*



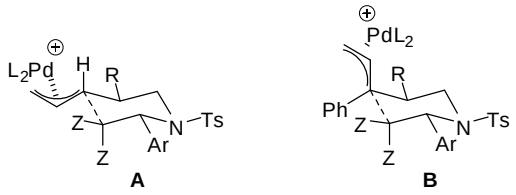
2,4-*cis* 2,4-*trans*

R^1	**R^2**	**R^3**	**R^4**	**Product**[a]	**Yield (dr)**[b]
Ph	H	H	Ph	**13a**	94 (>19:1)[c]
p-MeOC$_6$H$_4$	H	H	Ph	**13b**	88 (>19:1)
p-MeOC$_6$H$_4$	H	H	*p*-AcOC$_6$H$_4$	**13c**	81 (>19:1)
p-ClC$_6$H$_4$	H	H	Ph	**13d**	87 (>19:1)
p-ClC$_6$H$_4$	H	H	*p*-AcOC$_6$H$_4$	**13e**	96 (>19:1)
Ph	H	H	*p*-AcOC$_6$H$_4$	**13f**	76 (>19:1)
Ph	H	Ph	Ph	**13g**	54 (10:1)
Ph	H	Ph	*p*-AcOC$_6$H$_4$	**13h**	53 (>19:1)
Bn	H	H	Ph	**13i**	66 (8.3:1)
H	H	H	Ph	**13j**	85 (1:3)
H	H	H	*p*-AcOC$_6$H$_4$	**13k**	99 (1:2.8)
H	CH$_3$	H	Ph	**13l**	99 (1:2)
H	CH$_3$	H	*p*-AcOC$_6$H$_4$	**13m**	92 (1:2)
H	Ph	H	Ph	**13n**	87 (1:>19)

[a] Unless otherwise mentioned, the reaction was carried out with vinyl oxazinanone (1 mmol), Michael acceptor (1 mmol), Pd(PPh$_3$)$_4$ (0.05 mmol) in CH$_2$Cl$_2$ at room temperature. [b] yield and syn/anti ratio of isolated product. [c] >19:1 indicates that the minor diastereomer was not detected by ^{1}H NMR spectroscopy.

Although the preference for formation of 2,4-*trans* products, as determined by nOe experiments, from unsubstituted vinyl oxazinanones is difficult to explain, the diastereoselectivity of the substituted derivatives is straightforward. In these cases, the product is the result of cyclization through a conformation **A** or **B** that places the larger groups in equatorial positions as shown in Scheme 14. Such an interpretation requires that the Michael addition is reversible, allowing the diastereoselectivity to be controlled by the relative barriers for cyclization.

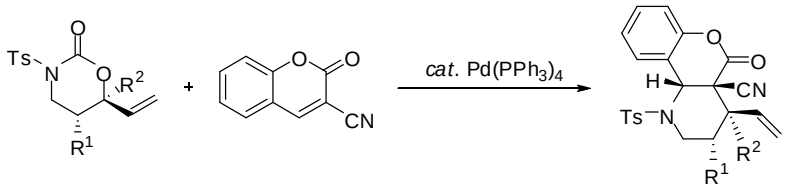
Scheme 14 *Preferred six-membered transition state*

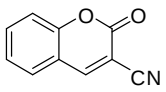


Furthermore, the above cycloaddition can be applied to an annulation of cyanocoumarins, which are frequently encountered structural motifs of many biologically active compounds (Table 2).[21, 22] Although product **16a** was isolated in lower yield than other substrates, investigation of the reaction by ^{1}H NMR spectroscopy shows clean formation of **16a**. Furthermore, the annulation sets three contiguous stereocenters with high diastereoselectivity for *syn* addition to the coumarin. Unlike entry 1 and 2, when R^2 equals to a phenyl group, decarboxylative cycloaddition product **16c** was produced along with the four-membered azetidine

product in a ratio of 2.5:1. The reason was partially attributed to the sterically bulkier vinyloxazinanone, which slows down the intermolecular cycloaddition reaction. For example, the reaction with unsubstituted vinyl oxazinanone took less than 10 minutes, whereas substituted ones need days to complete as shown in Table 2.

Table 2 *Yields and diastereoselectivities with cyanocoumarin Michael acceptor*



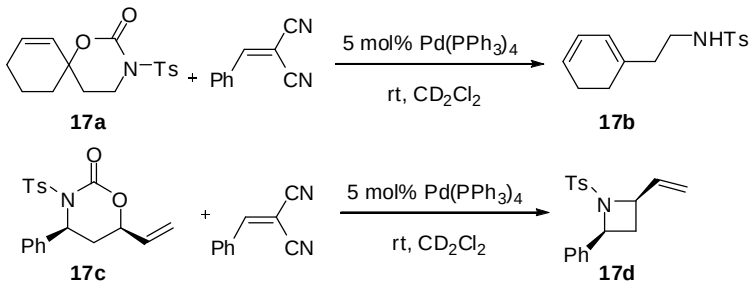
entry	R^1	R^2	Michael acceptor	Product[a]	time	Yield (dr)
1	H	H		**16a**	**10min**	49 (>19:1)[b]
2	H	CH_3		**16b**	**36 hr**	88 (1:1)
3	Ph	H		**16c**	**3 days**	71 (>19:1)[c]

[a] Unless otherwise mentioned, the reaction was carried out with vinyl oxazinanone (1 mmol), Michael acceptor (1 mmol), $Pd(PPh_3)_4$ (0.05 mmol) in CH_2Cl_2 at room temperature. [b] ^1H NMR yield are very high. [c] ^1H NMR yield and the reaction time is 3 days.

Spiro vinyl oxazinanone **17a** was treated with 5 mol% $Pd(PPh_3)_4$ in the presence of one equivalent of Michael acceptor; however, cycloaddition did not occurr and *β*-hydride elimination product **17b** was formed exclusively (Scheme 15). Interestingly, decarboxylative ring contraction product **17d** was yielded when *cis*-oxazinanone **17c** was employed under our standard reaction conditions. Noteworthy here is that the four-membered azetidine **17d** did not isomerize to the thermodynamically more stable tetrahydropyridine, which occurred smoothly without benzylidene malononitrile

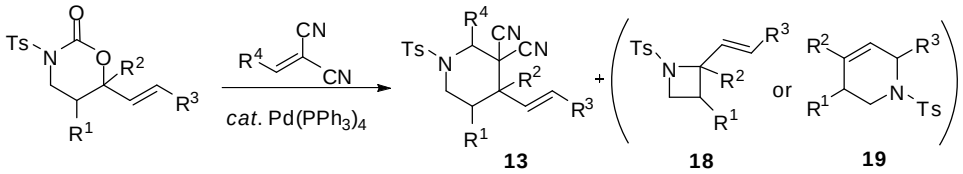
present. We have no reasonable explanation for why cycloaddition reaction did not occur with compound **17c**; however it may reside in steric effects brought by the *cis*-geometry of 4,6-substituents.

Scheme 15 *Substrates with no reactivity toward cycloadditions*



While **17c** is an extreme example, the decarboxylative ring contractions often competed with the cycloaddition reaction pathway as shown in Table 3. The lower yields of vinyl piperidines **13g** and **13h** were due to the formation of azetidine products (Table 1). In addition, a 1:1 mixture of **13o** and **18b** was formed with a bulky isopropyl substituted oxazinanone (entry 3).

Table 3 *Lower chemoselectivity with sterically hindered vinyl oxazinanones*

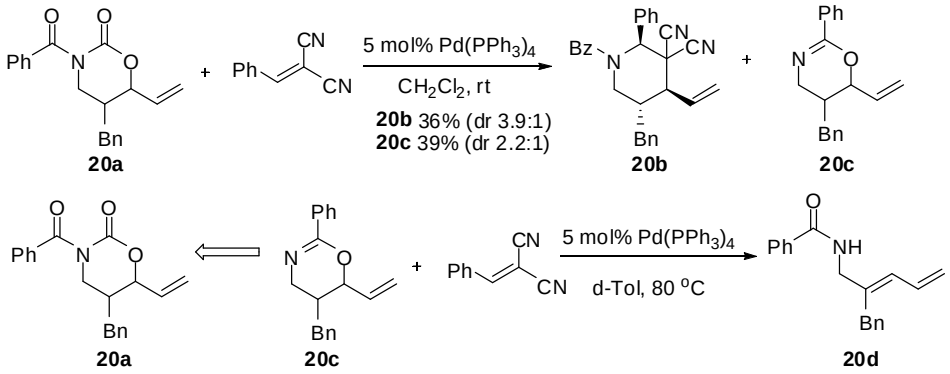


entry	R^1	R^2	R^3	R^4	Product[a]	ratio
1	Ph	H	Ph	Ph	**13g:18a**	2.3:1
2	Ph	H	Ph	*p*-$AcOC_6H_4$	**13h:18a**	1.7:1
3	$CH(CH_3)_2$	H	H	Ph	**13n:18b**	1:1
4	H	Ph	H	Ph	**13n:19a**[b]	7.5:1[c]

[a] Except for **3o**, 2,4-*cis* vinylpiperidine was the major diastereoisomer. [b] 6-membered decarboxlylative ring product **9a** was formed as the by-product. [c] the product ratio of scale-up reaction, while ^{1}HNMR reaction ratio was 2.5:1.

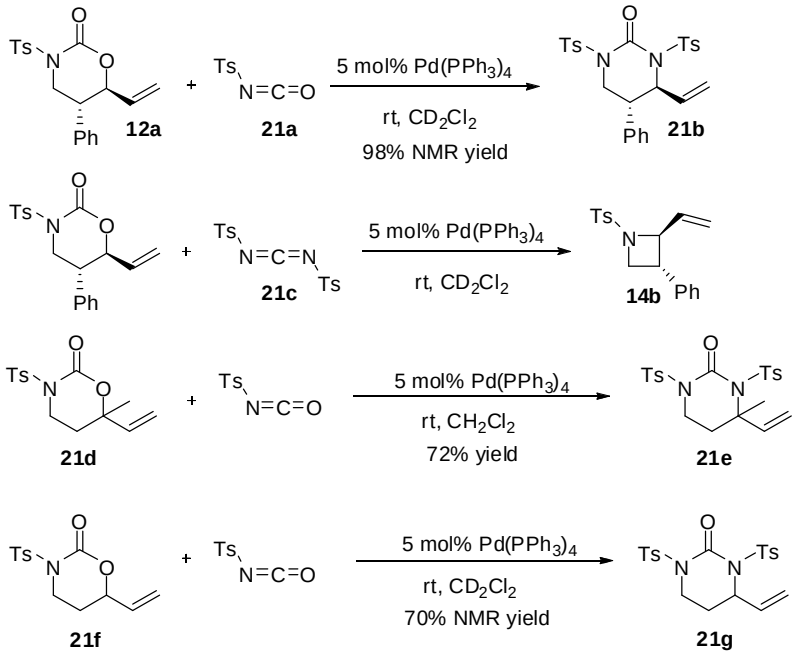
A benzoyl protected vinyl oxazinanone **20a** (1:1 cis/trans) was also employed in the decarboxylative cycloaddition reaction, which produced a mixture of cycloaddition product **20b** and decarboxylative allylation product **20c** (~1:1 ratio) as illustrated in Scheme 16. However, when compound **20c** was treated with a palladium catalyst in toluene at 80 ^{0}C in the presence of a Michael acceptor, *β*-hydride elimination product **20d** was generated formed without the formation of cycloaddition product **20b**.

Scheme 16 *Cycloaddition with Bz-protected vinyl oxazinanone*



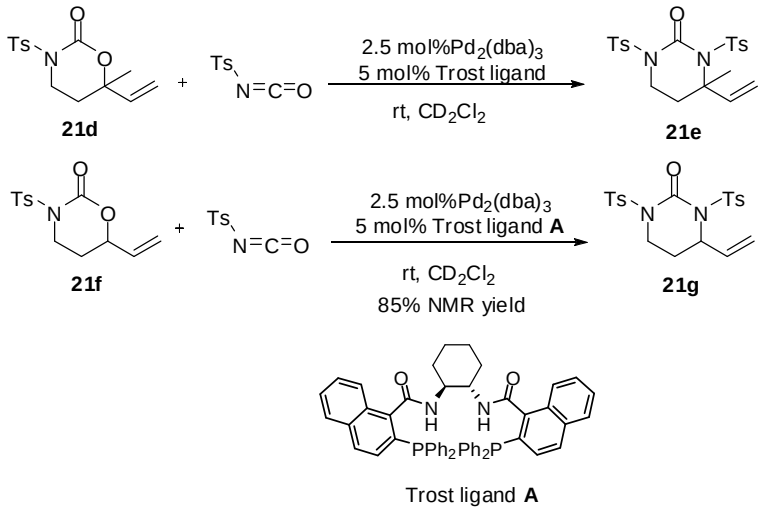
As a further extension of the above decarboxylative cycloadditions, we would like to develop an asymmetric version of this reaction protocol. Toward that end, vinyl oxazinanone **12a** was allowed to react with isocyanate **21a** and carbodiimide **21c** in the presence of 5 mol% $Pd(PPh_3)_4$ in dichloromethane at room temperature, in which cycloaddition product **21b** and ring contraction product **14b** were produced respectively as shown in Scheme 17. Other oxazinanones were also used and cycloaddtion products **21e** and **21g** were obtained in 72% and 70% yield respectively. Of note here is that the reactions with isocyanate were very sensitive to water and the solvent needed to be dried over basic anhydrous alumina to ensure the clean formation of cycloaddition products.

Scheme 17 *Cycloadditions of heterocumulenes*



The decarboxylative cycloadditions were also carried out in the presence of 5 mol% $Pd_2(dba)_3$ combined with 10 mol% of the Trost ligand (Scheme 18). With the Trost ligand, cycloaddition reactions were generally faster and cleaner than those catalyzed by $Pd(PPh_3)_4$. However, we had a hard time in separating compound **21e** and **21g** on chiral stationary phase HPLC (Diacel Chiralpak AD-H and OD-H) and the stereoselectivity of these reactions deserve further attention.

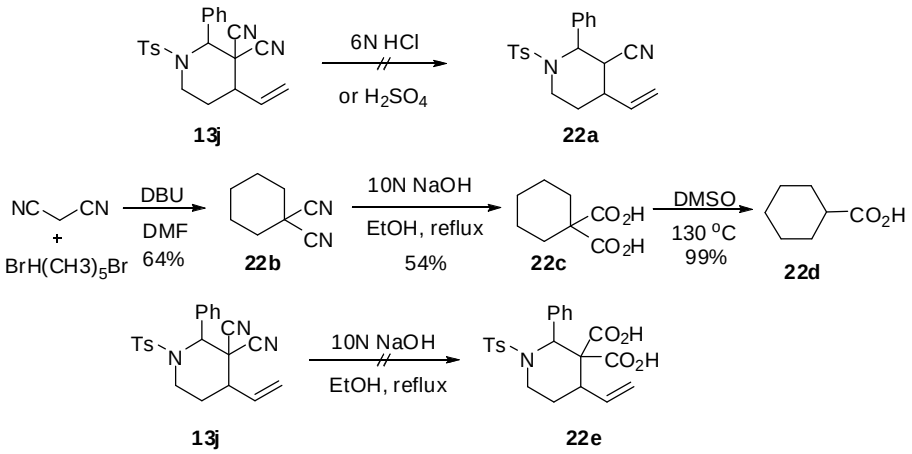
Scheme 18 *Asymmetric cycloadditions*



Trost ligand **A**

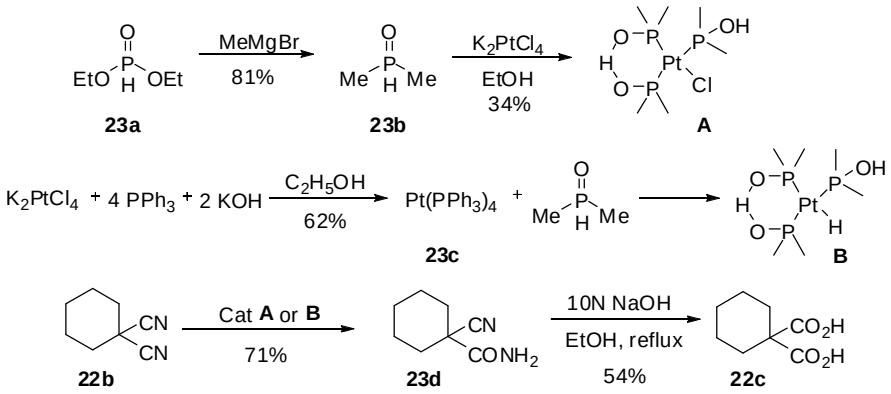
Finally, to investigate the utility of the malonotrile-containing products, we performed a hydrolysis and decarboxylation of **13j** to the mono cyano-substituted piperidine product as shown in Scheme 19. Acidic condition gave a mixture of starting material along with an unidentified new product; however the reaction did not go to completion, even at high temperature.[26, 27] An analogue, 1,1-cyclohexane dicarbonitrile **22b**, was then prepared and used as the standard substance for comparison. Treatment of **22b** with concentrated sodium hydroxide solution afforded the corresponding carboxylic acid **22c**, which upon decarboxylation gave **22d** in quantitative yield.[23] However, a messy mixture formed when **13j** was treated under the same reaction conditions.

Scheme 19 *Acid and base hydrolysis of nitriles*



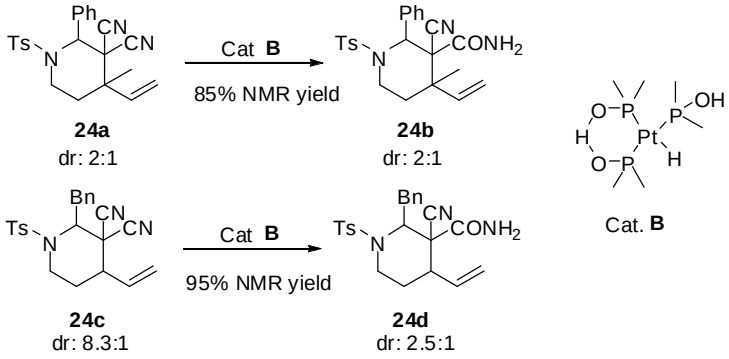
Platinum complexes **A** and **B** have been shown to catalyze the partial hydrolysis of nitriles to amides.[24] Treatment of 1,1-cyclohexanedicarbonitrile **22b** with 0.5 mol% catalyst **A** and **B** provided the amide product **23d** (Scheme 20). According to literature report, complex **B** was catalytically more active than **A**; however only one of the nitrile function group was selectively hydrolyzed in both cases to generate the corresponding cyanoamide product **23d**, which was further hydrolyzed to the dicarboxylacid **22c.**

Scheme 20 *Platinium complexes catalyzed nitriles hydrolysis*



Piperdine drivatives **24a** and **24c** were also subjected to the Pt-catalyzed nitrile hydrolysis, in which amide products **24b** and **24d** were formed smoothly as shown in Scheme 21. It is worthy to note that in both cases, a diastereoisomeric mixture was obtained cleanly.

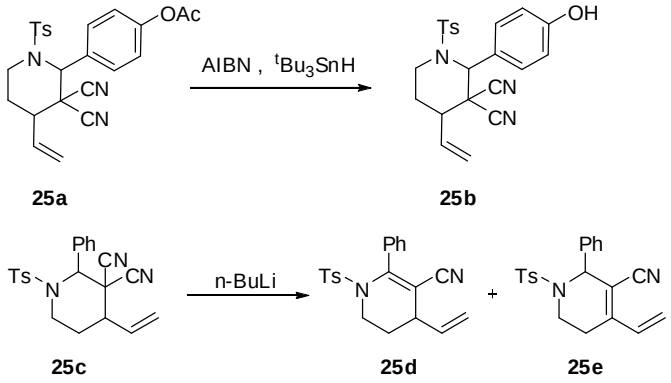
Scheme 21 *Pt- catalyzed nitriles hydrolysis with piperdine derivatives*



A radical process has previously been used to decyanate germinal dinitriles (Scheme 22).[25] Interestingly, treatment of piperdine **25a** with AIBN and *t*-butyl tin hydride generated the deacetylated product **25b** while the cyano groups remained

intact. Strong bases such as *n*-butyl lithium induced a *β*-elimination reaction to form diene product **25d** along with another product, whose structure was temporarily signed to be **25e**.

Scheme 22 *Other reaction conditions*



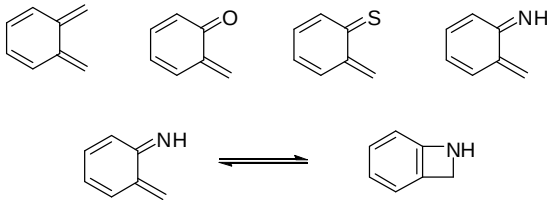
In summary, we have reported that decarboxylation of the vinyl oxazinanones in the presence of Michael acceptors results in cycloaddition to form highly substituted piperidines with good diastereoselectivity. Importantly, those reactions proceed under mild conditions and produce CO_2 as the only byproduct. We further demonstrated that the resulting geminal dinitriles can be transformed to the corresponding amides with resort to Pt-catalyzed nitrile hydrolysis.

3.3 Palladium-Catalyzed Asymmetric, Diastereoselective Cycloadditions in Hydroquinoline Synthesis

3.3.1 Methods for generating aza-ortho-xylylenes and applications in synthesis

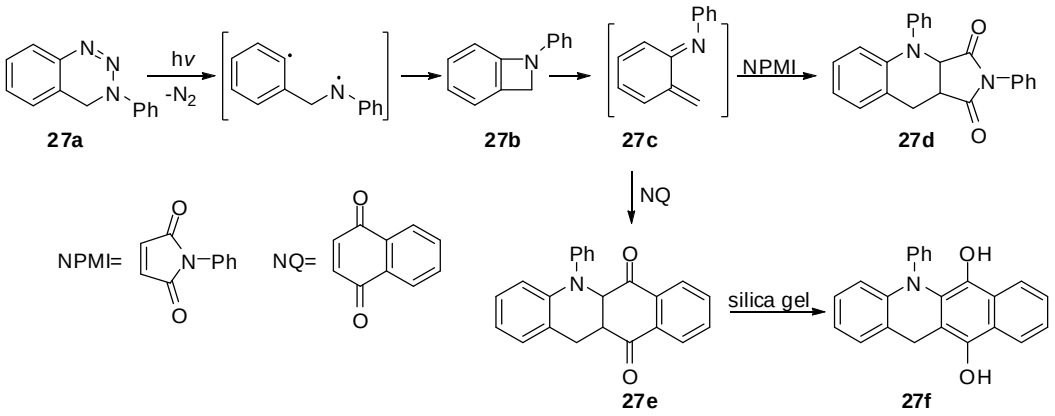
Aza-*ortho*-xylylenes like **26a** are highly reactive intermediates that have been used to construct nitrogen heterocycles ever since Smolinsky proposed the structure of aza-*ortho*-xylylene for the first time in 1961.[31, 32] Other xylyene analogues, such as the oxy- and thio-xylyenes are also known and have found many applications in heterocyclic ring syntheses (Scheme 23).[26, 27] Aza-*o*-xylylene **26a** could isomerize to benzoazetidine **26b**, during which the driving force is the rearomatization; however theoretical calculations at the MP2 level showed that isomer **26a** is more stable.[28]

Scheme 23 *Aza-ortho-xylylene and its analogues*



Preparation of aza-*ortho*-xylylene **27c** was achieved by treatment of benzoazetine **27b** with either thermal or photochemical conditions, followed by intermolecular Diels-Alder reaction with *N*-phenylmaleimide (NPMI) or 1,4-naphthoquinone (NQ) to give quinoline products **27d** and **27f** respectively as illustrated in Scheme 24.[29, 30]

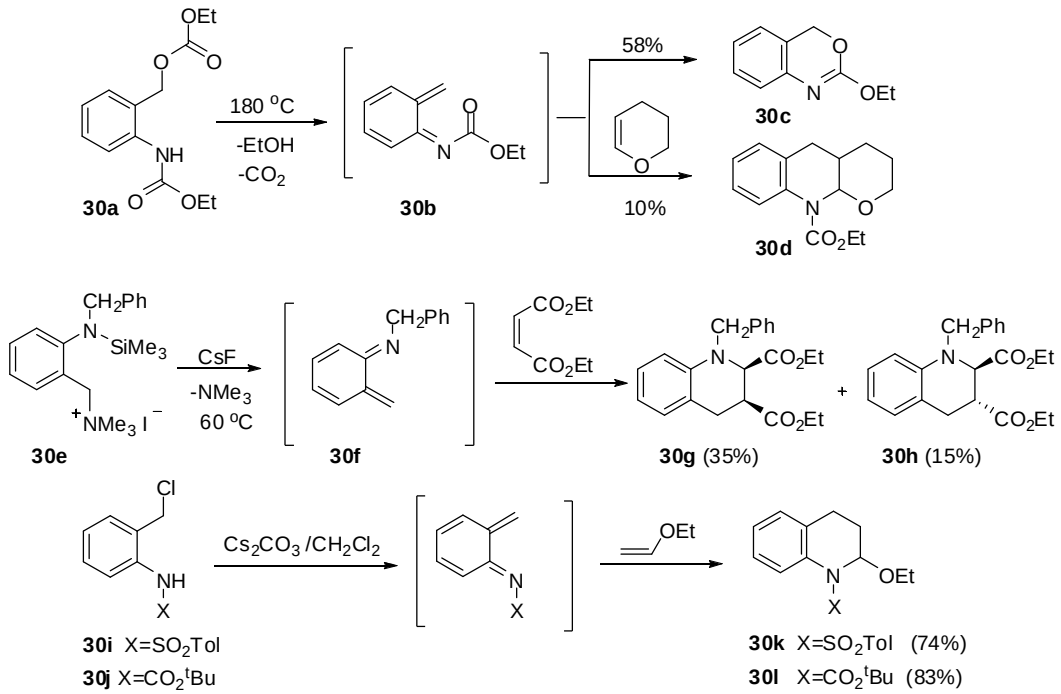
Scheme 24 *Reactions of Aza-ortho-xylylenes prepared from benzoazetine*



Another convenient strategy for generating aza-*ortho*-xylylenes is 1,4-emlination reactions of various 1,4-amino benzyl derivatives as illustrated in Scheme 27. Upon losing one molecule of ethanol and CO_2, aza-*ortho*-xylylene **30b** was formed from 1,4-amino benzyl carbonate **30a**, followed by a intramolecular 6π eletrocyclization reaction to furnish a benzoxazine derivative **30c** in 58% yield. In the presence of a dienophile, Diels-Alder adduct **30d** was obtained, albeit in low yield.[31] In 1986, Saegusa showed that a TMS-protected ammonium salt **30e** reacted with cesium fluoride to generate xylyene intermediate **30f** under mild reaction conditions, during which one molecule of trimethylamine was extruded. Cycloaddition with diethyl maleate generated the quinoline products **30g** and **30h** in combined 50% yield.[32] 1,4-Elimination of HCl from *o*-(chloromethyl)aniline derivatives has also been used for generating xylyenes. For instance, treatment of **30i** and **30j** with cesium carbonate produced aza-*ortho*-xylylenes intermediates, which then underwent cycloadditions

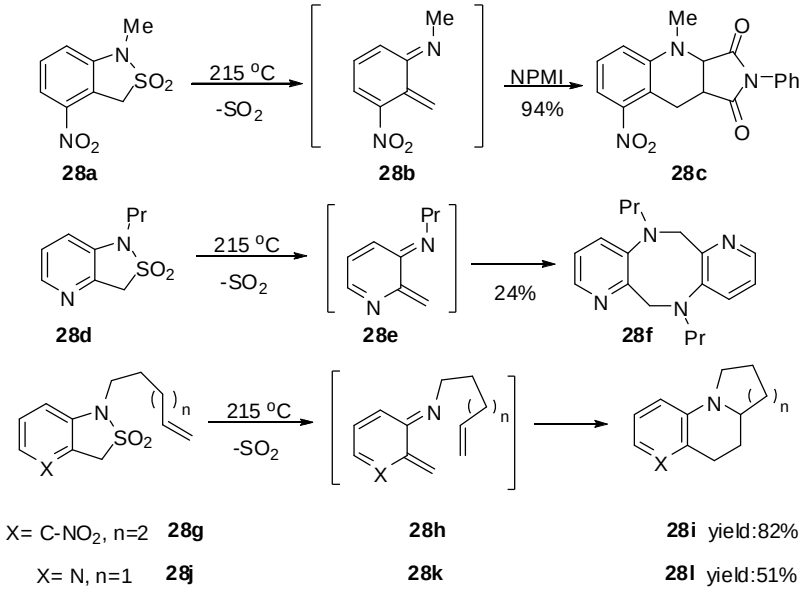
with vinyl ethyl ether to give quinoline products **30k** and **30l** in good yields.[40, 41]

Scheme 27 *Aza-ortho-xylylenes preparation via 1,4-emlimation reactions*



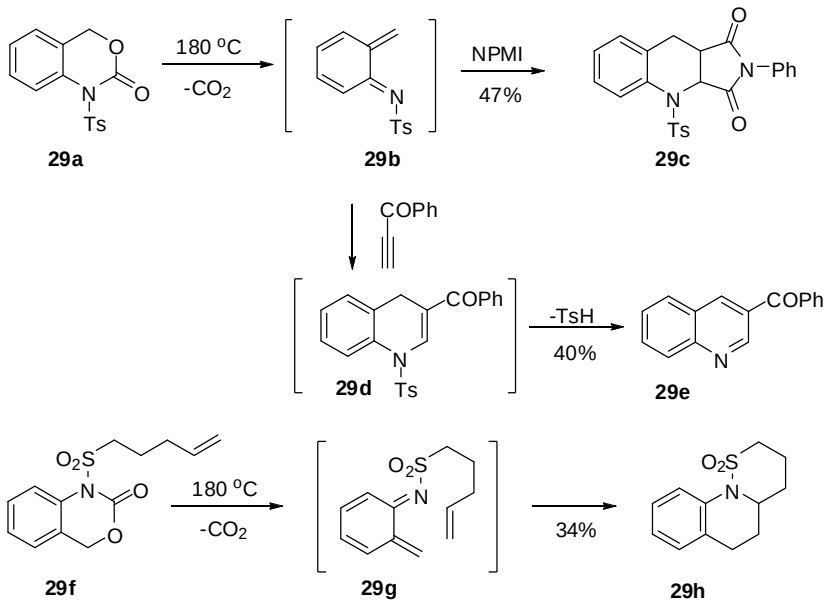
Benzosultams have also served as the precursor to aza-*ortho*-xylylenes upon losing one molecule of SO_2 as shown in Scheme 25. For instance, intermediate **28b** reacted with a dienophile NPMI to produce the corresponding [4+2] cycloaddition product **28c**, while a dimeric eight-membered diazocine **28f** was formed through a formal [4+4] cycloaddition in the absence of dienophiles.[33-35] The intramolecular Diels-Alder reactions of xylylene intermediates **28h** and **28k** were also investigated, in which the corresponding tetrahydroquinolines were synthesized in good yields.

Scheme 25 *Reactions of Aza-ortho-xylylenes generated from benzosultams*



Finally, and most relevant to this chapter, thermal decarboxylation of benzoxazinanones **29a** also results in the formation of aza-*ortho*-xylylenes such as **29b**; the aza-*o*-xylylene was trapped with different dienophiles to give the related Diels-Alder adducts **29c** and **29e** in moderate yields (Scheme 26). Similarly, treatment of benzoxazinanones **29f** with flash vacuum pyrolysis (FVP) at 180 ^{o}C produced aza-*ortho*-xylylene intermediates **29g**, which underwent an intramolecuar [4+2] cycloaddition to produce quinoline derivatives **29h** in moderate to low yield.[36]

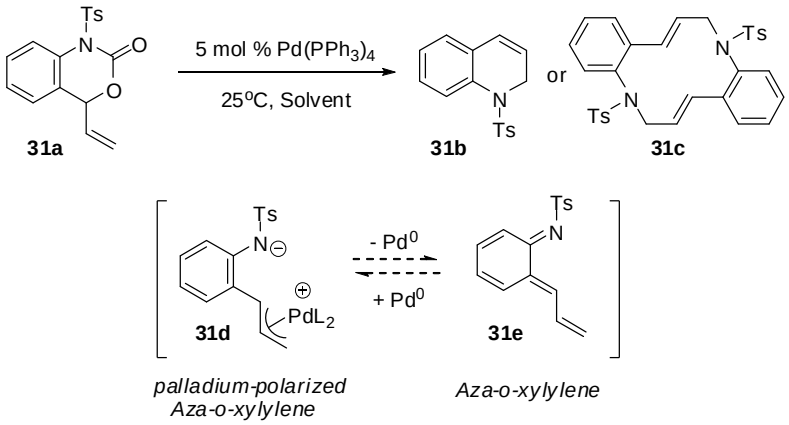
Scheme 26 *Reactions of Aza-ortho-xylylenes prepared from benzoxazinanones*



3.3.2 Palladium-facilitated aza-ortho-xylylene generation and its application in hydroquinoline synthesis

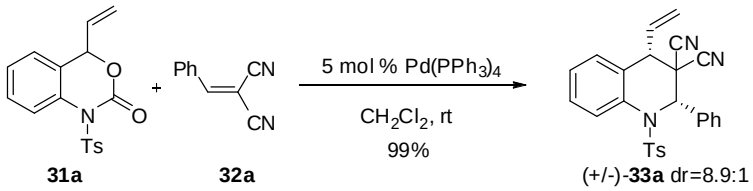
Recently, we have shown that catalytic decarboxylative cycloadditions of aza-*ortho*-xylenes occurs under mild conditions via zwitterionic π-allyl palladium intermediates (Scheme 28). This was discussed in chapter 2.[19] Two possible intermediates **31d** and **31e** were proposed to form from the decarboxylation of **31a** and our experimental results supported that palladium-polarized aza-*o*-xylylenes **31d** are likely the intermediates, considering the formation of dimer product **31c**. Next we wanted to develop a diastereoselective, asymmetric [4+2] cycloaddition of palladium-polarized aza-*o*-xylylenes with electron deficient olefins.

Scheme 28 *Zwitterionic π-allyl palladium intermediates*



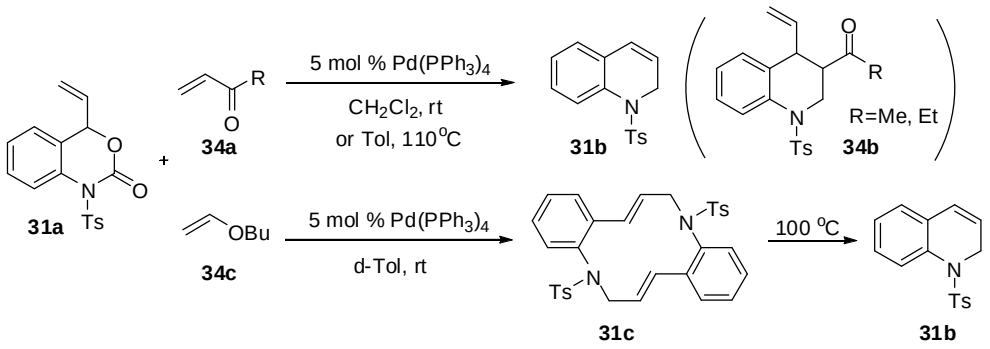
If zwitterionic Pd-allyl intermediates are indeed being formed, then one would also predict that they would undergo [4+2] cycloadditions with electron deficient olefins as shown in Scheme 29.[18, 37] Indeed, upon treatment of the benzoxazinanone **31a** with $Pd(PPh_3)_4$ in the presence of one equivalent of benzylidene malononitrile **32a**, cycloaddition occurs to produce the highly substituted dihydroquinoline **33a** with good diastereoselectivity. This reaction was also carried out in non-polar solvents such as toluene and cycloaddition adduct **33a** was afforded smoothly with no observation of the dimer formation.

Scheme 29 *[4+2] cycloaddition with electron deficient olefin*



To exclude the possibility that the free aza-*o*-xylenene intermediate is involved in the above [4+2] cycloaddition, different dienophiles **34a** and **34c** were allowed to react with vinyl benzoxazinanone **31a** catalyzed by 5 mol% $Pd(PPh_3)_4$ in either methylene chloride or toluene as shown in Scheme 30. Either of these electrophiles would be expected to react with a free aza-*o*-xylylene intermediate. The cycloaddition adducts such as **34b** were not formed in those reactions, which further confirmed that palladium-polarized aza-*o*-xylylenes are likely the relevant intermediates.

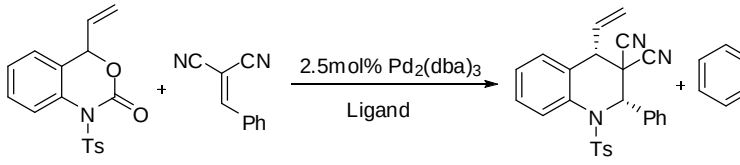
Scheme 30 *Other dienophiles do not undergo [4+2] cycloadditions*



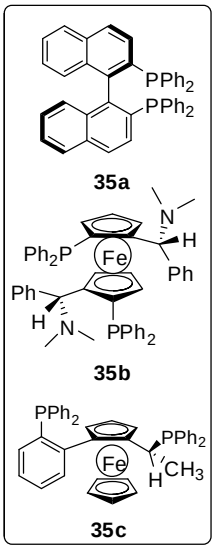
Next, we turned our attention toward the development of an asymmetric version of this cycloaddition. Standard ligand screening quickly revealed that the Trost-ligands are superior ligands for the asymmetric cycloaddition (Table 4).[38] While the diphenyldiamine-based ligand **35e** provided the highest enantioselectivity, the ligand based on the anthracenyl diamine **35g** provided high enantioselectivity as well

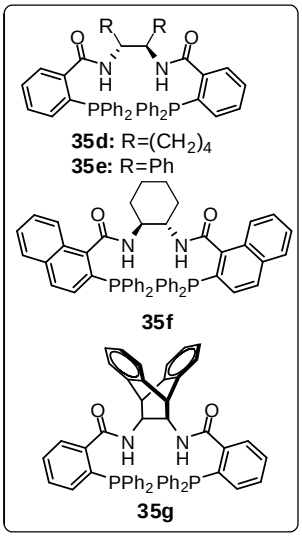
as superior diastereoselectivity. A single recrystallization of the product derived from **35g** provided an 87% yield of highly enantio- and diastereoenriched hydroquinoline (97% ee, 50:1 dr).

Table 4 *Ligand and solvent screening results*



Ligand	Sovlent	33a:31b	ee 33a	dr
35a	CD_2Cl_2	NR	-	-
35b	CD_2Cl_2	NR	-	-
35c	CD_2Cl_2	NR	-	-
35d	CD_2Cl_2	>19:1	78	**7:1**
35e	CD_2Cl_2	>19:1	92	**9:1**
35f	C_6D_6	1.7:1	78	**9.4:1**
35f	CH_2Cl_2	0.85:1	69	**6:1**
35f	THF	5.5:1	69	>19:1
35g	C_6D_6	10.6:1	88	15:1
35g	CH_2Cl_2	>19:1	89[a]	19:1[a]
35g	THF	>19:1	89	32:1
35g	dioxane	>19:1	87	21:1



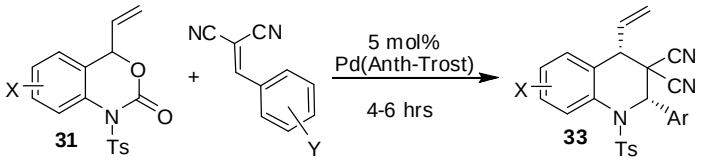


[a] 97% ee and 50:1 dr after a single recrystallization.

Using these as standard reaction conditions, we briefly explored the effect of electronics on the reaction. If the benzylidene malononitrile was too electron rich [i.e. *p*-$MeOC_6H_4CHC(CN_2)$] then the intermolecular cycloaddition did not compete with the intramolecular cyclization to form dihydroquinolines.[39, 40] However, if the olefin was sufficiently electron deficient, then the cycloaddition proceeded with both high

enantioselectivity and diastereoselectivity; the ee's and dr's of the product dihydroquinolines before recrystallization are shown in Table 5. Highly electron-deficient olefins slowed the reaction substantially, presumably due to favorable binding to the Pd(0) catalyst.[41] For example, in contrast to most reactions which were facile at room temperature, the nitro-containing benzylidene malononitrile (**33b-33d**, Table 5) required 80 °C for the reaction to proceed. It is noteworthy that the reaction selectivity was largely unaffected by the increased reaction temperature.

Table 5 *Asymmetric decarboxylative cycloaddition of vinyl oxazinanones.*[a]

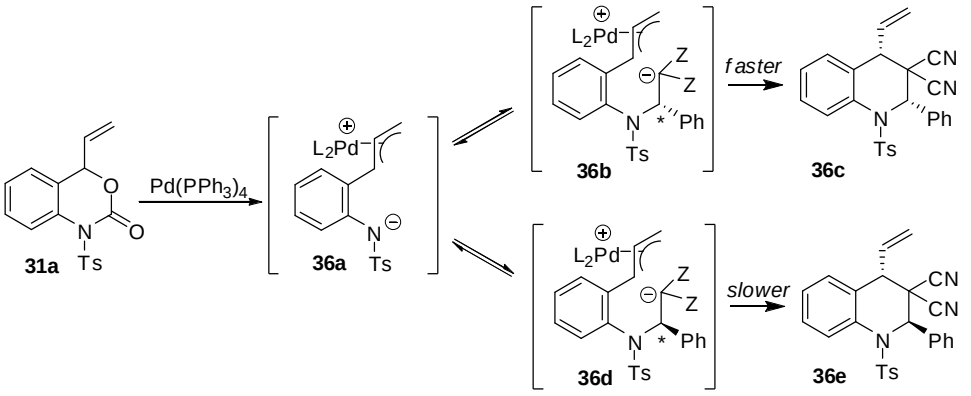


Product	X	Y	Yield	ee	dr
33b[b]	*p*-OMe	*p*-NO_2	91	99	25:1
33c[b]	*p*-Me	*p*-NO_2	90	99	>99:1
33d[c]	H	*p*-NO_2	78	96	>99:1
33e	*p*-OMe	*p*-CO_2Me	99	92	25:1
33f	*p*-Me	*p*-CO_2Me	97	98	37:1
33g	H	*p*-CO_2Me	76	96	25:1
33h	*p*-OMe	*o*-CF_3	97	86	29:1
33i	*p*-Me	*o*-CF_3	85	98	>99:1
33j	H	*o*-CF_3	78	89	36:1
33k	*p*-OMe	*p*-CF_3	93	84	37:1
33l	*p*-Me	*p*-CF_3	88	86	56:1
33m	H	*p*-CF_3	90	91	45:1
33n	*p*-OMe	*p*-OAc	90	80	50:1
33o	*p*-Me	*p*-OAc	73	90	70:1
33p	H	*p*-OAc	52	91	92:1
33q	*p*-F	*p*-OAc	60	87	>99:1
33r	*p*-OMe	H	92	86	54:1
33s	*p*-Me	H	77	92	>99:1
33t	*p*-F	H	75	87	87:1

[a] 1.0 mmol substrate was treated with $Pd_2(dba)_3$ (0.025 mmol) and **35g** (0.055 mmol) in CH_2Cl_2 at room temperature. [b] run in CH_2Cl_2 at 40 °C for 25 h. [c] run in toluene at 80 °C for 6 h.

The origin of the stereoselectivity in this reaction is not known, however the reaction likely proceeds through aza-Michael addition of intermediate **36a** to the activated olefin (Scheme 31). The resulting stabilized carbanionic intermediate can then undergo intramolecular cyclization. The two potential stereochemistry--determining steps in such a transformation are 1) the aza-Michael addition or 2) the cyclization. Since it is difficult to imagine that the chirality of the ligands could effect a highly enantioselective aza-Michael addition, our working hypothesis is that reversible conjugate addition is followed by stereochemistry-determining cyclization. This hypothesis is consistent with the pKa values for malononitrile (11.2) and the arylsulfonamide (9-10).[42]

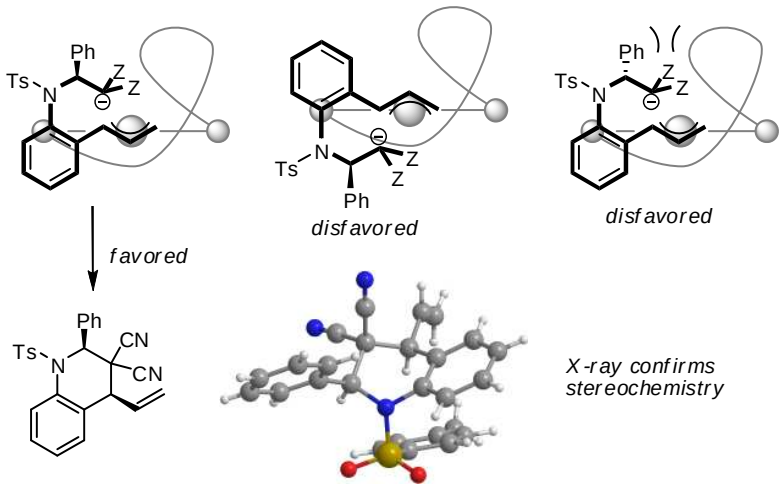
Scheme 31 *The origin of the reaction's stereoselectivity*



Curtin-Hammett analysis of the resulting kinetic scenario indicates that the major product of the reaction will result from the most favorable cyclization.[43] Elegant studies have allowed Lloyd-Jones to develop a model for the binding of Trost ligands

to palladium.[44] These studies suggest that Trost ligand binds to produce a complex of C1-symmetry where the ligand bulk is concentrated in the upper right-hand and lower left-hand quadrants. Superimposing our intermediate onto Lloyd-Jones' model gives four potential transition states for cyclization; three are shown in Scheme 32. The favored transition state results from placing the benzylidene malononitrile fragment in the least hindered quadrant and the phenyl group is directed away from the bulky ligand in back. Such a prediction is confirmed by an X-ray crystal structure of the product that is of sufficient quality to allow determination of the relative and absolute configuration of the product.

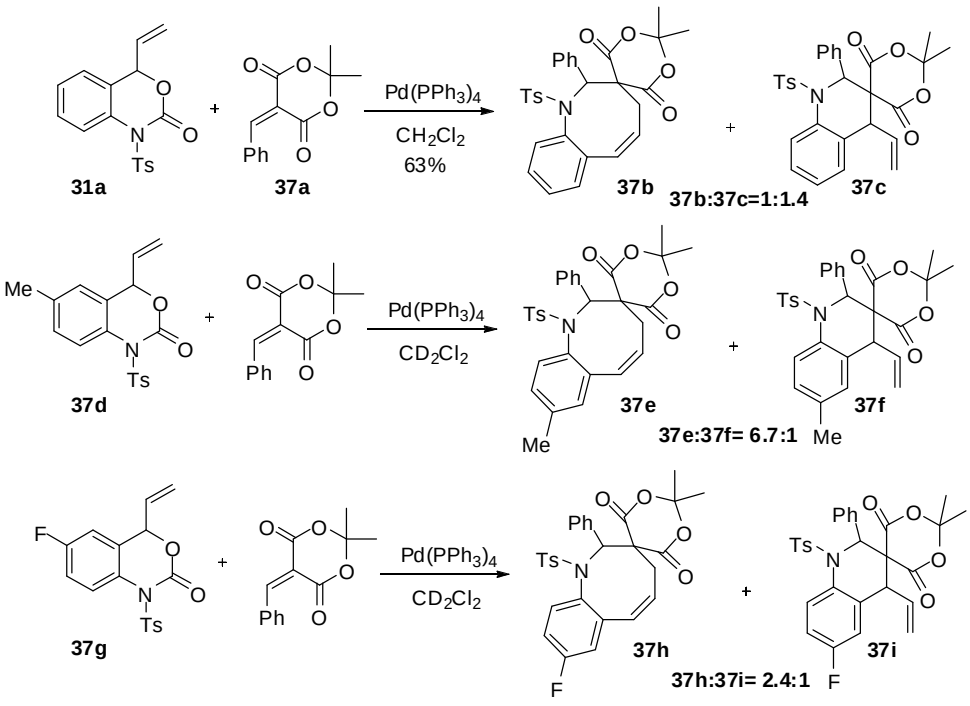
Scheme 32 *Possible transition states for cyclizations*



Other electron deficient olefins were also tested to check their compatibility. Meldrum's acid derivative **37a** has been shown to be a suitable reactant for both

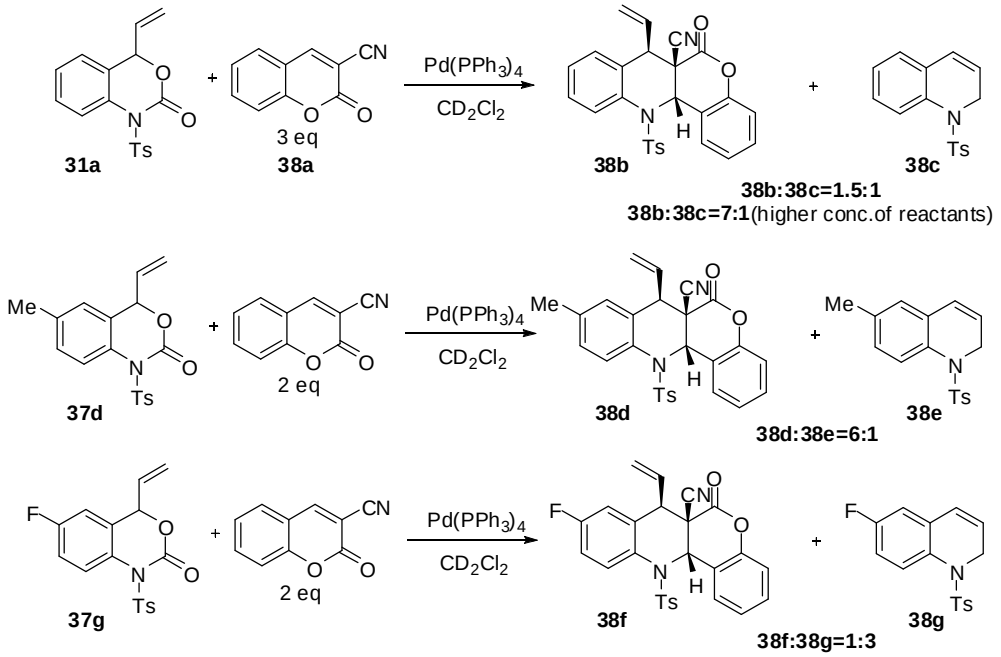
Ru-catalyzed tandem Michael addition-allylic alkylations and Pd-catalyzed decarboxylative olefin insertions with vinyl oxazinanones.[19, 20] Interestingly, when compound **37a** was allowed to react with different vinyl benzoxazinanones, a mixture of six- and eight-membered ring products was generated in different ratios (Scheme 33). Of note here is that Meldrum's acid derivative **37a** is very reactive and those reactions were done in less than 10 minutes without observing any dihydroquinoline formation. However cycloaddition reactions became much slower with $Pd_2(dba)_3$ and anthracenyl diamine Trost ligand and a polymer-like product was generated. Since the asymmetric decarboxylative cycloaddition reactions were only realized during the formation of terminal olefins, that research was not further carried on.

Scheme 33 *Six-membered vs eight-membered cycloaddition products*



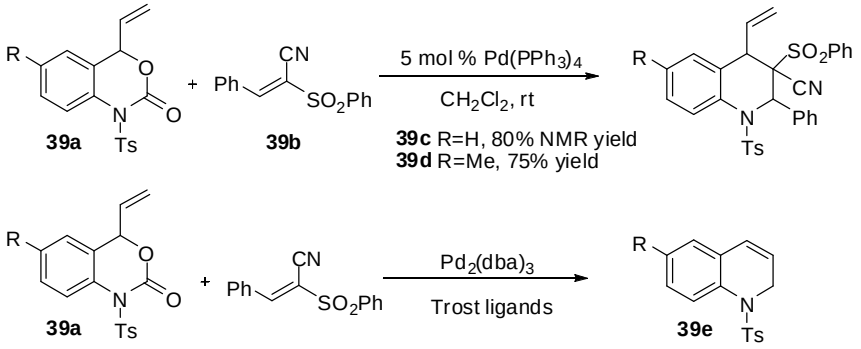
In addition, the above cycloadditions can be applied to the annulation of cyanocoumarins, which are frequently encountered structural motifs of many biologically active compounds.[21, 22] For example, vinyl benzoxazinanone **31a** reacted with three equivalents of cyanocourmarin **38a** in the presence of $Pd(PPh_3)_4$ to yield a mixture of cycloadducts and dihydroquinolines in a ratio of 1.5:1, which can be improved to 7:1 by carrying out the reaction at higher concentration as shown in Scheme 34. Varying the electronics of the benzoxazinanones did not produce significant beneficial effects plus polymer-like byproducts were always formed along with dihydroquinolines. The optimization of those reaction conditions was not performed but could warrant further attention.

Scheme 34 *[4+2] cycloadditions with cyanocoumarin*



Regarding to the substrate scope, electron deficient olefin **39b** was allowed the react with benzoxazinanone **39a** (Scheme 35). Even though racemic cycloaddition products were formed smoothly in two hours at room temperature, dihydroquinolines along with polymer byproducts were formed when the same reaction were catalyzed by $Pd_2(dba)_3$ and different Trost ligands in a much slower rate. Even though we are not exactly sure about the reason, it could reside in two factors. First, it is known that phenylsulfonyl group is bulkier than the corresponding cyano group and thus slow down the cycloaddition step. Secondly, phenylsulfonyl has been shown to function as a ligand for palladium catalysts. Consequently, the competition of ligand binding between Trost ligands and **39b** may favor the intramolecular cyclization.[45, 46]

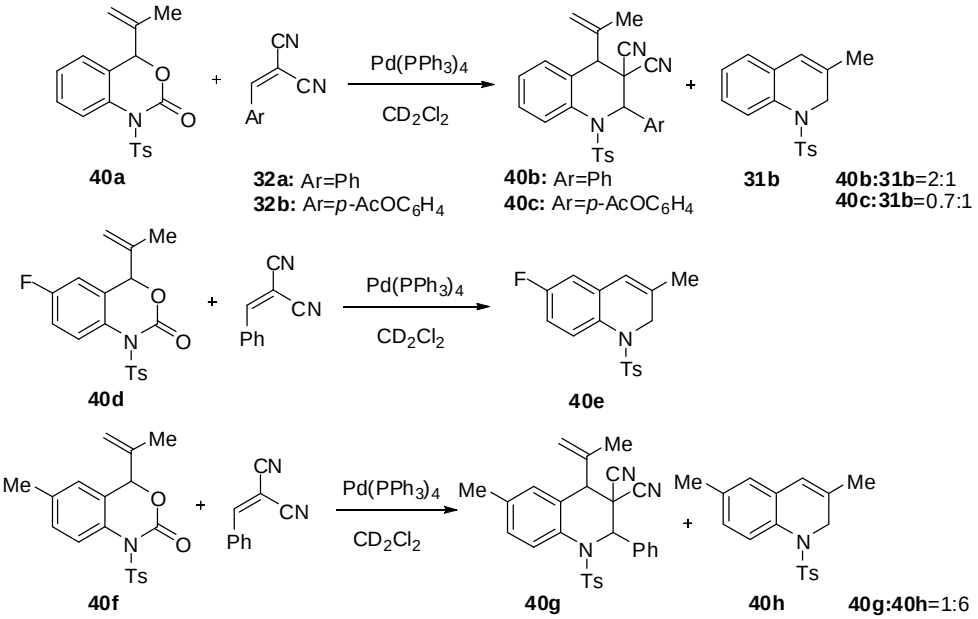
Scheme 35 *[4+2] cycloadditions with other electron deficient olefins*



Vinyl benzoxazinanones **40a** with a methyl substituent on the olefin were allowed to react with electron deficient olefins, generating a mixture of cycloaddition product **40b** and dihydroquinoline **31b** with poor chemoselectivity, even though

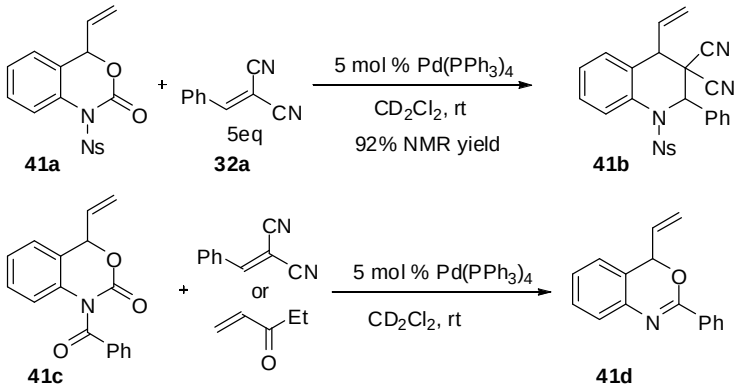
generally those reactions were clean with no occurrence of dimer by-products (Scheme 36). Vinyl benzoxazinanones **40d** yielded dihydroquinoline **40e** exclusively, while compound **40h** was obtained as the major product from **40f**.

Scheme 36 *[4+2] cycloadditions with substitute* v*inyl benzoxazinanones*



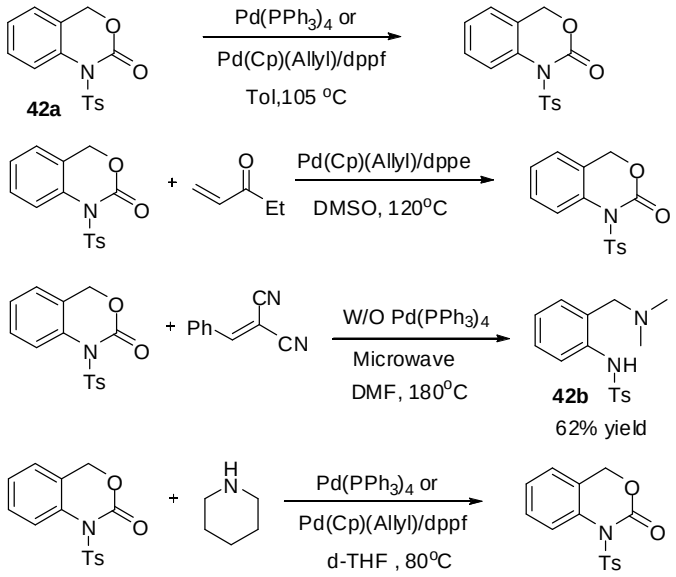
Cycloadditions of vinyl benzoxazinanones with different *N*-protecting groups were also performed (Scheme 37). For example, nosyl-protected substrate formed product **41b** smoothly at the cost of requiring excess of olefin **32a**. The analogous [4+2] cycloadditions of benzoyl-protected benzoxazinanone **41b** did not afford the corresponding cycloadducts and intramolecular cyclization occurred to give product **41d**.

Scheme 37 *Vinyl benzoxazinanones with different N-protecting groups*



The generation of aza-*ortho*-xylylene intermediate was proven to be very difficult with substrate **42a**, which remained intact in most cases (Scheme 38). Interestingly, when benzoxazinanone **42a** was allowed to react with benzylidene malononitrile under microwave irridation in DMF at 180 ^{o}C, a diamine product **42b** was generated in high yield with or without the palladium catalyst. Other solvents would have been planned but the Microwave reactor broke down. Trapping the aza-*o*-xylylene intermediates with amines was also tried and starting material was recovered.

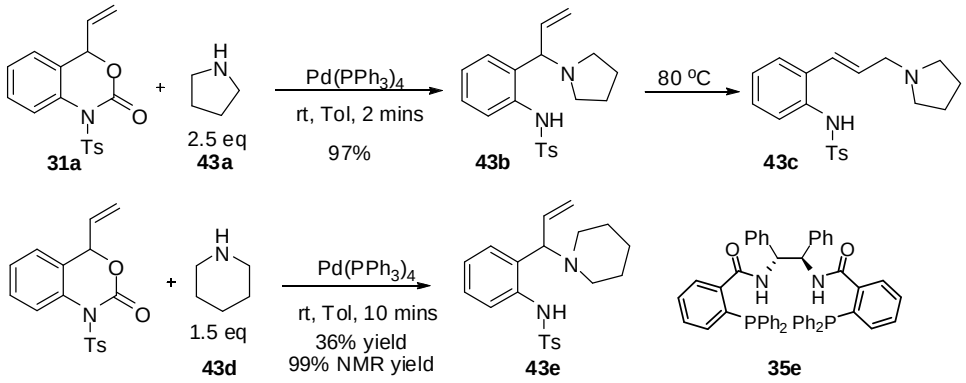
Scheme 38 *Reactions of traditional benzoxazinanone*



Trapping aza-*o*-xylenene intermediates with good nucleophiles has been reported.[47-49] Similarly, secondary amines have been used in our experiments as shown in Scheme 39. The secondary amines **43a** and **43d** turned out to be so reactive that those reactions were finished in less than 10 minutes and a control experiment without palladium catalyst was also performed to generate product **43e** in less than an hour. Such reactivity was later proven to be problematic when benzoxazinanone **31a** was allowed to react with piperidine **43d** in the presence of $Pd_2(dba)_3$ and Trost ligand **35e**, which produced product **43e** as a racemic mixture. Interestingly, those reactions displayed different regioselectivity from traditional Pd-catalyzed allylic alkylations. In our case, the terminal olefins **43b** and **43e** were formed exclusively, and at higher

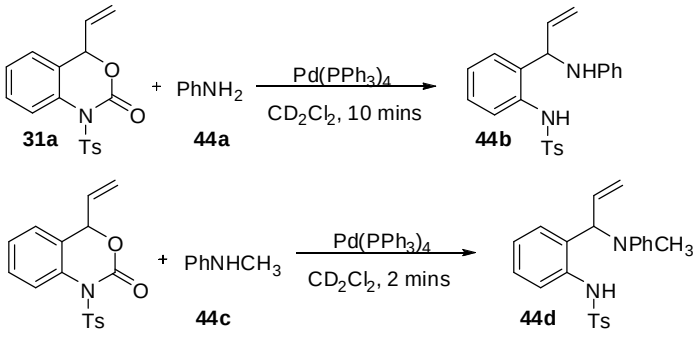
temperature, terminal olefin product **43b** isomerized to the more thermodynamically stable product **43c**.

Scheme 39 *Allylic aminations via Aza-o-xylenene intermediates*



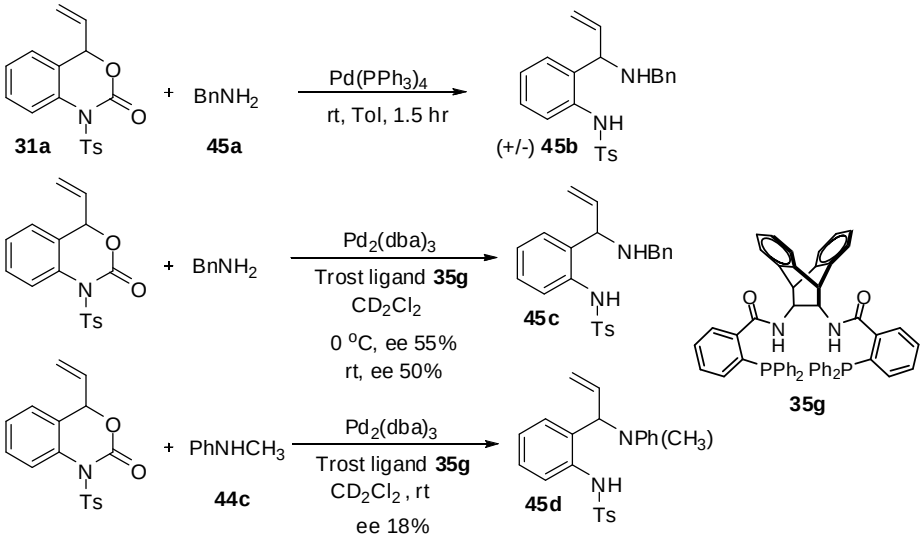
Aniline derivatives were allowed to reacted with benzoxazinanone **31a** in the presence of $Pd(PPh_3)_4$ and addition products **44b** and **44d** were obtained in less than 20 minutes (Scheme 40); however the products were not stable and transformed into polymer-like by-products upon standing overnight. This reaction did not occur without palladium catalyst and was very sluggish in toluene.

Scheme 40 *Allylic aminations via Aza-o-xylenene intermediates*



A racemic diamine product **45b** was prepared by treatment of benzylamine with benzoxazinanone **31a** in the presence of 5 mol% $Pd(PPh_3)_4$ as shown in Scheme 41. With anthracenyl diamine Trost ligand **35g**, enantioenriched product **45b** was obtained (55% and 50% ee at 0 ^oC and 25 ^oC respectively), while the ee of aniline derivative **45d** was very low. We reasoned that electron-poor amines such as cyanopyrrole could potentially give a better enantioselectivity because of its lower nucleophilicity, which deserves further attention.

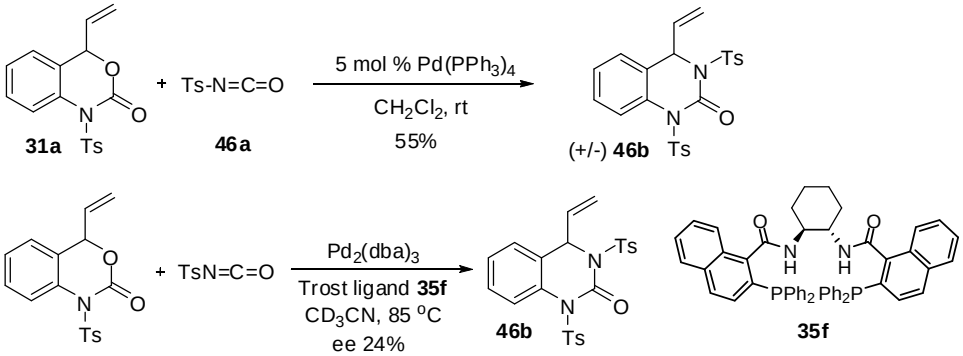
Scheme 41 *Asymmetric allylic aminations*



To further expand the scope of asymmetric [4+2] cycloadditions, tosyl isocyanate was allowed to react with treated vinyl benzoxazinanone **31a** as shown in Scheme 42. Even though racemic mixture **46b** was formed cleanly in 55% isolated yield, the asymmetric reaction gave the cycloaddition product in 24% ee at higher temperature.

Other Trost ligands combined with $Pd_2(dba)_3$ generated a messy mixture of dihydroquinoline and polymer byproducts.

Scheme 42 *[4+2] cycloadditions with tosyl isocyanate*



In conclusion, we have developed an asymmetric decarboxylative cycloaddition that proceeds through intermediates that may be viewed as palladium-polarized aza-*ortho*-xylylenes. Formal [4+2] cycloaddition of these intermediates produces enantioenriched hydroquinolines with high diastereoselectivity. The implied stabilization of aza-*o*-xylylenes by palladium is expected to translate to other reactive intermediates.

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Appendix C

Experimental Procedures and Data for Chapter 3

General Experimental

THF was dried over sodium metal. Toluene, methylene chloride and diethyl ether were dried over activated alumina on a solvent system purchased from Innovative Technology, Inc.[1] Acetonitrile and 1,4-dioxane were dried and stored over activated molecular sieves. Commercially available reagents were used without additional purification unless otherwise stated. Products were purified on silica gel from Sorbent Technologies (230x400 mesh, 60 Å porosity, pH 6.5-7.5). Ruthenium and palladium compounds were obtained from Strem. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5715-7, EMD chemicals). UV lamp (254 nm) or $KMnO_4$ stain were used for monitoring TLC plates.

^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance 400 or Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals. Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, and HMQC spectroscopies and X-ray data. High resolution mass spectrometry was performed on an AUTOSPEC-Q tandem hybrid mass spectrometer (VG Analytical Ltd, Manchester, UK). High resolution mass spectrometry was performed on a LCT Premier (Waters Corp., Milford MA) time of flight mass spectrometer. FTIR spectra were acquired on a Shimadzu FTIR-8400S spectrometer. HPLC analysis was performed on a Shimadzu SCL-10A VP instrument.

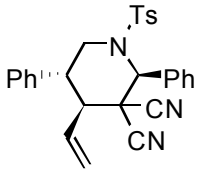
Preparation of Starting Materials

Vinyl oxazinanones were prepared as reported in Chapter 2 of this thesis.

General procedure for catalytic decarboxylative olefin insertions:

In a Schlenk tube under argon, $Pd(PPh_3)_4$ (0.05 mmol) and carbamate **1** (1 mmol), and different Michael acceptors (1 mmol) were dissolved in 5 mL of methylene chloride. The resulting yellow solution was stirred at ambient temperature under Ar until reaction completion was indicated by TLC. Following solvent evaporation, the crude product was purified via flash chromatography (SiO2, 5:1 Hexane: Ethyl acetate).

Spectroscopic Data



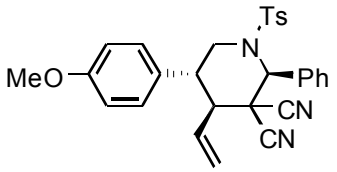
2,5-diphenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile
13a(cw2027)
colorless oil
$Pd(PPh_3)_4$: 94% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 3H: arom H), 7.38 (m, 7H: arom H), 7.18 (d, 2H, *J* =6.8 Hz: arom H), 7.06 (d, 2H, *J* =8.6 Hz: arom H), 5.93 (s, 1H: PhC**H**NTs), 5.62 (m, 1H: CH_2=C**H**), 5.20 (dd, 2H, *J* =10.4, 16.9 Hz: =C**H**$_2$), 3.99 (dd, 1H, *J* =4.5, 13.4 Hz: C**H**$_2$NTs), 3.39 (m, 1H: C**H**$_2$NTs), 3.25 (m, 2H: overlapping PhC**H**, C**H**CH=CH_2), 2.35 (s, 3H: C**H**$_3$Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.36 (Quat.), 137.84 (Quat), 135.27 (Quat.), 133.91 (Quat.), 132.12 (=**C**H), 130.26-127.81 (Arom.**C**H), 124.47 (=**C**H_2), 113.79 (**C**N), 113.31 (**C**N), 61.54 (Ph**C**HNTs), 47.51 (**C**H_2), 45.80/43.83 (overlapping Ph**C**H, **C**HCH=CH_2), 45.07 (**C**CN_2), 21.91 (**C**H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3090, 3065, 3034, 2251, 1599, 1497, 1354, 1167, 806, 758, 663.

HRMS calcd for $C_{28}H_{26}N_3O_2S$ [M+H] 468.1746, found 468.1737.



5-(4-methoxyphenyl)-2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

13b(cw2139)

colorless oil

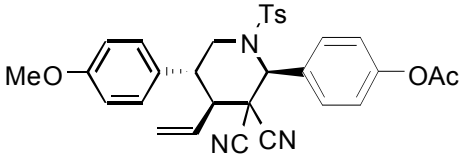
$Pd(PPh_3)_4$: 88% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (m, 4H: arom H), 7.38 (t, 4H, *J* =8.3 Hz: arom H), 7.09 (m, 4H: arom H), 6.90 (d, 2H, *J* =8.6 Hz: arom H), 5.92 (s, 1H: PhC**H**NTs), 5.61 (m, 1H: CH_2=C**H**), 5.21 (dd, 2H, *J* =10.4, 17.2 Hz: =C**H**$_2$), 3.97 (dd, 1H, *J* = 4.5, 12.6 Hz: C**H**$_2$NTs), 3.82 (s, 3H: OC**H**$_3$), 3.35 (dd, 1H, *J* =5.8, 12.9 Hz: C**H**$_2$NTs), 3.19 (m, 2H: overlapping ArC**H**, C**H**CH=CH_2), 2.35 (s, 3H: C**H**$_3$Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.71 (Quat.), 144.32 (Quat), 135.26 (Quat.), 132.93 (Quat.), 132.26 (=**C**H), 130.24-127.81 (Arom.**C**H), 124.38 (=**C**H$_2$), 114.94 (Arom.**C**H), 113.81 (**C**N), 113.34 (**C**N), 61.53 (Ph**C**HNTs), 55.72 (O**C**H$_3$), 47.66 (**C**H$_2$), 45.96/43.00 (overlapping Ar**C**H, **C**HCH=CH_2), 45.12 (**C**CN$_2$), 21.91 (**C**H$_3$Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3092, 3061, 3035, 2253, 1514, 1456, 1354, 1167, 814, 762, 660.

HRMS calcd for $C_{29}H_{27}N_3O_3SNa$ [M+Na] 520.1671, found 520.1652.



4-(3,3-dicyano-5-(4-methoxyphenyl)-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13c(cw2143)

colorless oil

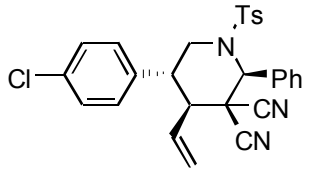
$Pd(PPh_3)_4$: 81% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, 2H, *J* =8.6 Hz: arom H), 7.37 (d, 2H, *J* =6.8 Hz: arom H), 7.10 (m, 6H: arom H), 6.91 (d, 2H, *J* =8.6 Hz: arom H), 5.92 (s, 1H: PhC**H**NTs), 5.60 (m, 1H: CH_2=C**H**), 5.22 (dd, 2H, *J* =10.4, 16.9 Hz: =C**H**$_2$), 3.96 (dd, 1H, *J* =4.3, 12.6 Hz: C**H**$_2$NTs), 3.82 (s, 3H: OC**H**$_3$), 3.20 (m, 3H: overlapping C**H**$_2$NTs, ArC**H**, C**H**CH=CH_2), 2.36 (s, 6H: overlapping C**H**$_3$Ts, OCO**C**H$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.14 (O**C**OCH$_3$), δ 159.72 (Quat.), 152.04 (Quat), 144.59 (Quat.), 135.03 (Quat.), 132.12 (=**C**H), 131.22-127.72 (Arom.**C**H), 124.49 (=**C**H$_2$), 122.76 (Arom.**C**H), 114.94 (Arom.**C**H), 113.68 (**C**N), 113.29 (**C**N), 60.89 (Ph**C**HNTs), 55.72 ((O**C**H$_3$), 47.62 (**C**H$_2$), 45.85/42.95 (overlapping Ph**C**H, **C**HCH=CH$_2$), 45.10 (**C**CN$_2$), 21.90/21.61 (overlapping **C**H$_3$Ts, OCO**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3089, 3034, 2251, 1769, 1610, 1514, 1354, 1167, 833, 660.

HRMS calcd for $C_{31}H_{29}N_3O_5SNa$ [M+Na] 578.1726, found 578.1730.



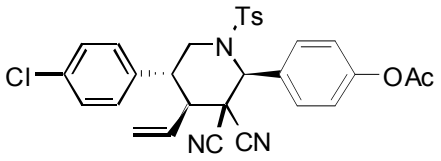
5-(4-chlorophenyl)-2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile
13d(cw2091)
colorless oil
$Pd(PPh_3)_4$: 87% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (m, 9H: arom H), 7.13-7.06 (m, 4H: arom H), 5.93 (s, 1H: PhC**H**NTs), 5.60 (m, 1H: CH$_2$=C**H**), 5.27 (d, 1H, *J* =10.4 Hz: =C**H**$_2$), 5.16 (d, 1H, *J* =16.9 Hz: =C**H**$_2$), 3.97 (dd, 1H, *J* = 4.3, 12.9 Hz: C**H**$_2$NTs), 3.24 (m, 3H: overlapping C**H**$_2$NTs, ArC**H**, C**H**CH=CH$_2$), 2.35 (s, 3H: C**H**$_3$(Ts)).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.47 (Quat.), 136.32 (Quat), 135.20 (Quat.), 134.50 (Quat.), 133.77 (Quat.), 131.84 (=**C**H), 130.31-127.78 (Arom.**C**H), 124.78 (=**C**H$_2$), 113.67 (**C**N), 113.15 (**C**N), 61.48 (Ph**C**HNTs), 47.36 (**C**H$_2$), 45.85 (**C**HCH=CH$_2$), 44.99 (**C**CN$_2$), 43.30 (Ar**C**H), 21.92 (**C**H$_3$Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3091, 3062, 3035, 2255, 1599, 1493, 1354, 1167, 1092, 831, 663.

HRMS calcd for $C_{28}H_{24}ClN_3O_2SNa$ [M+Na] 524.1175, found 524.1163.



4-(5-(4-chlorophenyl)-3,3-dicyano-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13e(cw2099)

colorless oil

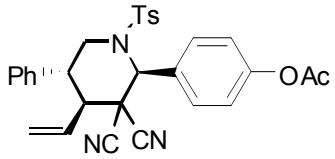
$Pd(PPh_3)_4$: 96% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 2H, *J* =8.2 Hz: arom H), 7.28 (t, 4H, *J* =8.5 Hz: arom H), 7.02 (m, 6H: arom H), 5.84 (s, 1H: PhC**H**NTs), 5.50 (m, 1H: CH_2=C**H**), 5.18 (d, 1H, *J* =10.4 Hz: =C**H**$_2$), 5.08 (d, 1H, *J* =17.0 Hz: =C**H**$_2$), 3.89 (dd, 1H, *J* =4.4, 12.9 Hz: C**H**$_2$NTs), 3.15 (m, 2H: overlapping C**H**$_2$NTs, ArC**H**), 3.02 (t, 1H, *J* =9.1 Hz: C**H**CH=CH_2), 2.27/2.26 (s, 6H: overlapping C**H**$_3$(Ts), OCO**C**H_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.67 (O**C**OCH_3), 151.70 (Quat.), 144.32 (Quat), 144.59 (Quat.), 135.81/134.70/134.18 (Quat.), 131.30 (=**C**H), 130.71-127.34 (Arom.**C**H), 124.46 (=**C**H_2), 122.40 (Arom.**C**H), 113.12 (**C**N), 112.71 (**C**N), 60.45 (Ph**C**HNTs), 46.93 (**C**H_2), 45.42 (**C**HCH=CH_2), 44.54 (**C**CN_2), 42.87 (Ar**C**H), 21.49/21.17 (overlapping **C**H_3Ts, OCO**C**H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3090, 3032, 2253, 1751, 1601, 1495, 1348, 1163, 1092, 813.

HRMS calcd for $C_{30}H_{26}N_3O_4SClNa$ [M+Na] 582.1230, found 582.1223.



4-(3,3-dicyano-5-phenyl-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13f(cw2033)

colorless oil

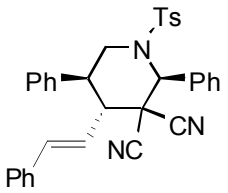
$Pd(PPh_3)_4$: 76% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, 2H, *J* =8.8 Hz: arom H), 7.40 (m, 5H: arom H), 7.18 (d, 2H, *J* =8.1 Hz: arom H), 7.13 (m, 5H: arom H), 5.94 (s, 1H: PhC**H**NTs), 5.61 (m, 1H: CH_2=C**H**), 5.22 (dd, 2H, *J* =10.4, 16.7 Hz: =C**H**$_2$), 3.99 (dd, 1H, *J* =4.3, 12.9 Hz: C**H**$_2$NTs), 3.31 (dd, 1H, *J* =11.4, 24.2 Hz: C**H**$_2$NTs), 3.20 (m, 2H: overlapping PhC**H**, C**H**CH=CH_2), 2.36/2.35 (s, 6H: overlapping C**H**$_3$Ts, OCOC**H**$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.09 (O**C**OCH$_3$), δ 152.07 (Quat.), 144.61 (Quat), 137.74 (Quat.), 135.11 (Quat.), 131.98 (=**C**H), 131.22-127.74 (Arom.**C**H), 124.55 (=**C**H$_2$), 122.76 (Arom.**C**H), 113.65 (**C**N), 113.25 (**C**N), 60.91 (Ph**C**HNTs), 47.71 (**C**H$_2$), 45.71/43.78 (overlapping Ph**C**H, **C**HCH=CH$_2$), 45.04 (**C**CN$_2$), 21.88/21.58 (overlapping **C**H$_3$Ts, OCO**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3090, 3065, 3034, 2251, 1767, 1599, 1497, 1354, 1167, 814, 660.

HRMS calcd for $C_{30}H_{27}N_3O_4SNa$ [M+Na] 548.1620, found 548.1620.



2,5-diphenyl-4-styryl-1-tosylpiperidine-3,3-dicarbonitrile

13g (cw2124)

colorless oil

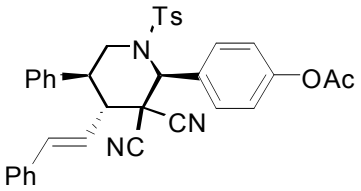
$Pd(PPh_3)_4$: 54% yield, dr = 10:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.08 (19H: arom H), 6.44 (d, 1H, *J* =15.7 Hz: =C**H**Ph), 5.96 (s, 1H: C**H**Ar), 5.92 (dd, 1H, *J* =8.6, 15.7 Hz: =C**H**), 4.03 (m, 1H: C**H**$_2$NTs), 3.38 (3H: overlapping C**H**$_2$NTs, PhC**H**, C**H**CH=CH), 2.37 (s, 3H: C**H**$_3$(Ts)).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.38 (Quat.), 138.74 (=**C**HPh), 137.85 (Quat.), 135.80 (Quat.), 135.30 (Quat.), 133.98 (Quat.), 130.28-127.10 (Arom.**C**H), 122.95 (=**C**H), 113.95 (**C**N), 113.34 (**C**N), 61.66 (Ph**C**HNTs), 47.61 (**C**H$_2$), 45.52 (**C**CN$_2$), 45.38 (**C**HCH=CH$_2$), 44.28 (**C**HPh), 21.93 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3067, 3032, 2253, 1769, 1599, 1497, 1354, 1165, 974, 814, 758, 663.

HRMS calcd for $C_{34}H_{29}N_3O_2SNa$ [M+Na] 566.1878, found 566.1874.



4-(3,3-dicyano-5-phenyl-4-styryl-1-tosylpiperidin-2-yl)phenyl acetate

13h (cw2152)

colorless oil

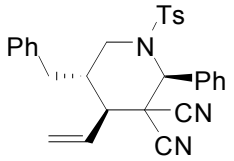
$Pd(PPh_3)_4$: 53% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, 2H, *J* =8.8 Hz: arom H), 7.39 (d, 2H, *J* =8.3 Hz: arom H), 7.36 (d, 2H, *J* =7.6 Hz: arom H), 7.30-7.19 (m, 8H: arom H), 7.14 (t, 4H: arom H), 6.47 (d, 1H, *J* =15.9 Hz: =C**H**Ph), 5.98 (s, 1H: C**H**Ar), 5.91 (dd, 1H, *J* =8.3, 15.7 Hz: =C**H**), 4.06 (dd, 1H, *J* =3.8, 12.6 Hz: C**H**$_2$NTs), 3.36 (m, 3H: overlapping C**H**$_2$NTs, PhC**H**, C**H**CH=CH), 2.37 (s, 6H: overlapping C**H**$_3$Ts, OCOC**H**$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.15 (O**C**OCH$_3$), δ 152.08 (Quat.), 144.65 (Quat), 138.84 (=**C**HPh), 137.73 (Quat.), 135.76 (Quat.), 135.08 (Quat.), 131.27-127.12 (Arom.**C**H), 122.82 (=**C**H), 113.83 (**C**N), 113.29 (**C**N), 61.03 (Ar**C**HNTs), 47.59 (**C**H$_2$), 45.52 (**C**HCH=CH$_2$), 45.27 (**C**CN$_2$), 44.22 (**C**HPh), 21.92/21.63 (overlapping **C**H$_3$Ts, OCO**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3084, 3061, 3032, 2255, 1769, 1599, 1508, 1354, 1271, 1167, 976, 816, 762, 694.

HRMS calcd for $C_{36}H_{31}N_3O_4SNa$ [M+Na] 624.1933, found 624.1934.



5-benzyl-2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

13i (cw2178)

colorless oil

$Pd(PPh_3)_4$: 66% yield, dr =8.3:1

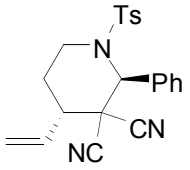
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 10H: arom H), 7.08 (m, 4H: arom H), 5.82 (m, 2H: overlapping PhC**H**NTs, CH$_2$=C**H**), 5.58 (dd, 2H, *J* =10.4, 16.9 Hz: =C**H**$_2$), 3.57 (dd, 1H, *J* =5.1, 13.9 Hz: C**H**$_2$NTs), 2.98 (m, 2H: overlapping C**H**$_2$NTs, C**H**$_2$Ph),

2.83 (t, 1H, J =9.1 Hz: C**H**CH=CH_2), 2.38 (m, 4H: overlapping C**H**$_3$Ts, C**H**$_2$NTs), 2.12 (m, 1H: C**H**Bn).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.28 (Quat.), 137.17 (Quat), 135.19 (Quat.), 133.88 (Quat.), 132.03 (=**C**H), 130.06-127.45 (Arom.**C**H), 125.16 (=**C**H_2), 113.98 (**C**N), 113.47 (**C**N), 61.22 (Ph**C**HNTs), 46.78/44.63 (overlapping **C**HCH=CH_2, **C**CN_2), 44.68 (**C**H_2NTs), 37.42/37.26 (overlapping Ph**C**H_2, Bn**C**H), 21.95 (**C**H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3055, 3030, 2252, 1599, 1495, 1354, 1169, 814, 762, 663.

HRMS calcd for $C_{28}H_{26}N_3O_2S$ [M+NH_4] 499.2168, found 499.2163.



2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

13j (cw2157)

colorless oil

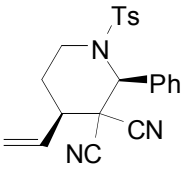
$Pd(PPh_3)_4$: 85% yield, dr =1:3

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 5H: arom H), δ 7.31 (d, 2H, J =7.6 Hz: arom H), 7.07 (d, 2H, J =8.1 Hz: arom H), 5.86 (m, 1H: CH_2=C**H**), 5.80 (s, 1H: PhC**H**), 5.41 (d, 1H, J = 10.4 Hz: CH=C**H**(H)$_Z$), 5.35 (d, 1H, J = 16.9 Hz: CH=C**H**(H)$_E$), 3.94 (m, 1H: C**H**$_2$NTs), 3.40 (m, 1H: C**H**$_2$NTs), 3.02 (m, 1H: C**H**CH=CH_2), 2.35 (s, 3H: C**H**$_3$Ts), 2.03 (m, 1H: C**H**$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.35 (Quat.), 135.26 (Quat.), 133.96 (Quat.), 133.79 (=**C**H), 130.15-127.82 (Arom.**C**H), 122.24 (=**C**H_2), 113.59 (**C**N), 113.43 (**C**N), 61.55 (**C**HPh), 44.40 (**C**CN_2), 40.99 (**C**H_2NTs), 40.42 (**C**HCH=CH_2), 26.55 (**C**H_2), 21.91 (**C**H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3059, 3036, 2254, 1599, 1495, 1350, 1165, 814, 760, 663.

HRMS calcd for $C_{22}H_{21}N_3O_2SNa$ [M+Na] 414.1252, found 414.1246.



2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

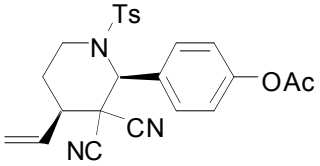
13j (cw2157)

colorless oil

$Pd(PPh_3)_4$: 85% yield, dr =1:3

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 5H: arom H), δ 7.30 (d, 2H, *J* =6.8 Hz: arom H), 7.20 (d, 2H, *J* =8.1 Hz: arom H), 5.88 (m, 1H: CH_2=C**H**), 5.45 (d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_Z$), 5.41 (d, 1H, *J* = 16.7 Hz: CH=C**H**(*H*)$_E$), 4.73 (s, 1H: PhC**H**), 4.03 (m, 1H: C**H**$_2$NTs), 3.48 (m, 1H: C**H**$_2$NTs), 2.68 (m, 1H: C**H**CH=CH_2), 2.43 (s, 3H: C**H**$_3$Ts), 2.23 (m, 1H: C**H**$_2$), 2.01 (m, 1H: C**H**$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.72 (Quat.), 135.71(Arom.**C**H), 133.76 (Quat.), 133.32 (=**C**H), 130.27-127.99 (Arom.**C**H), 122.27 (=**C**H_2), 114.18 (**C**N), 112.56 (**C**N), 66.19 (**C**HPh), 47.08 (**C**HCH=CH_2), 46.42 (**C**CN_2), 44.20 (**C**H_2NTs), 26.47 (**C**H_2), 21.98 (**C**H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.



4-(3,3-dicyano-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13k (cw2163)

colorless oil

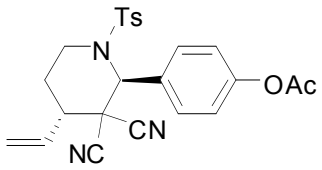
$Pd(PPh_3)_4$: 99% yield, dr =1:2.8

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 4H: arom H), δ 7.23 (d, 2H, *J* =8.3 Hz: arom H), 7.01 (d, 2H, *J* =8.8 Hz: arom H), 5.86 (m, 1H: CH_2=C**H**), 5.44(d, 1H, *J* = 9.3 Hz: CH=C**H**(*H*)$_Z$), 5.42 (d, 1H, *J* = 16.2 Hz: CH=C**H**(*H*)$_E$), 4.71 (s, 1H: ArC**H**), 4.06 (m, 1H: C**H**$_2$NTs), 3.47 (m, 1H: C**H**$_2$NTs), 2.70 (m, 1H: C**H**CH=CH_2), 2.42 (s, 3H: C**H**$_3$Ts), 2.33 (s, 3H: C**H**$_3CO_2$), 2.23 (m, 1H: C**H**$_2$), 2.02 (m, 1H: C**H**$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.13 (O**C**OCH_3), δ 152.13 (Quat.), 144.84 (Quat), 135.79 (Quat.), 133.26 (=**C**H), 130.90-127.92 (Arom.**C**H), 122.35 (=**C**H_2), 121.94 (Arom. **C**H), 113.99 (**C**N), 112.48 (**C**N), 65.81 (**C**HAr), 47.22 (**C**HCH=CH_2), 46.40 (**C**CN_2), 44.28 (**C**H_2NTs), 26.55 (**C**H_2), 21.63 (overlapping **C**H_3Ts, **C**H_3CO_2). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3063, 2253, 1762, 1597, 1508, 1354, 1169, 816.

HRMS calcd for $C_{24}H_{23}N_3O_4SNa$ [M+Na] 472.1307, found 472.1305.



4-(3,3-dicyano-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13k (cw2163)

colorless oil

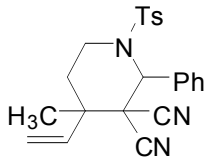
$Pd(PPh_3)_4$: 99% yield, dr =1:2.8

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, 2H, *J* =8.1 Hz: arom H), δ 7.39 (d, 2H, *J* =8.8 Hz: arom H), 7.13 (d, 2H, *J* =8.3 Hz: arom H), 7.06 (d, 2H, *J* =8.6 Hz: arom H), 5.85 (m, 1H: CH_2=C**H**), 5.82 (s, 1H: ArC**H**), 5.42 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_Z$), 5.39 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_E$), 3.95 (td, 1H, *J* =3.5, 12.9 Hz: C**H**$_2$NTs), 3.34 (m, 1H: C**H**$_2$NTs), 2.95 (q, 1H, *J* =7.6, 16.2 Hz: C**H**CH=CH_2), 2.36 (s, 3H: C**H**$_3$Ts), 2.32 (s, 3H: C**H**$_3CO_2$), 2.02 (m, 1H: C**H**$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.14 (O**C**OCH_3), δ 151.98 (Quat.), 144.60 (Quat), 135.08 (Quat.), 133.64 (=**C**H), 131.31-127.78 (Arom.**C**H), 122.60 (Arom. **C**H), 122.35 (=**C**H_2), 113.42 (**C**N), 113.36 (**C**N), 60.90 (**C**HAr), 44.43 (**C**CN_2), 40.90 (**C**H_2NTs), 40.43 (**C**HCH=CH_2), 26.54 (**C**H_2), 21.90/21.58 (overlapping **C**H_3Ts, **C**H_3CO_2). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3062, 2253, 1769, 1599, 1508, 1350, 1165, 816.

HRMS calcd for $C_{24}H_{23}N_3O_4SNa$ [M+Na] 472.1307, found 472.1294.



4-methyl-2-phenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

13l (cw2200)

colorless oil

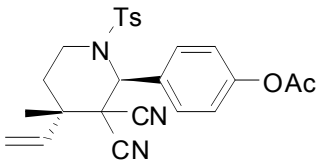
$Pd(PPh_3)_4$: 99% yield, dr =1:2

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 8H: arom H), 7.23 (m, 3H: arom H), 7.15 (m, 3H: arom H), 6.12 (dd, 1H, *J* =10.9, 17.2 Hz: CH_2=C**H,** major isomer), 5.86 (dd, 0.5H, *J* =10.9, 17.2 Hz: CH_2=C**H,** minor isomer), 5.49 (dd, 2H, *J* =10.9, 17.4 Hz: =C**H**$_2$, major isomer), 5.28 (dd, 1H, *J* =14.4, 17.2 Hz: =C**H**$_2$, minor isomer), 5.15 (s, 0.5H: PhC**H**, minor isomer), 4.95 (s, 1H: PhC**H**, major isomer), 3.95 (m, 1.5H: C**H**$_2$NTs), 3.75 (m, 1.5H: C**H**$_2$NTs), 2.40 (s, 4.5H: C**H**$_3$Ts), 2.28 (m, 1.5H: C**H**$_2$), 2.02 (m, 1.5H: C**H**$_2$), 1.48 (s,1.5H: C**H**$_3$, minor isomer), 1.41 (s, 3H: C**H**$_3$, major isomer).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.31 (Quat.), 138.97 (=**C**H, minor isomer), 137.38 (=**C**H, major isomer), 136.47 (Quat.), 136.08 (Quat.), 133.70 (Quat.), 133.48 (Quat.), 129.84-127.81 (Arom. **C**H), 120.09 (=**C**H_2, major isomer), 118.12 (=**C**H_2, minor isomer), 113.84 (**C**N), 113.57 (**C**N), 62.50, 61.85 (**C**HPh), 50.82, 50.34 (**C**CN_2), 43.35, 42.72 (Quat.), 41.66, 41.37 (**C**H_2NTs), 31.71, 31.42 (**C**H_2), 25.14, 23.39 (**C**H_3), 21.97 (**C**H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3060, 2250, 1597, 1496, 1384, 1161, 814, 661.

HRMS calcd for $C_{23}H_{24}N_3O_2S$ [M+H] 406.1598, found 406.1563.



4-(3,3-dicyano-4-methyl-1-tosyl-4-vinylpiperidin-2-yl)phenyl acetate

13m (cw2205)

colorless oil

$Pd(PPh_3)_4$: 99% yield, dr =1:2

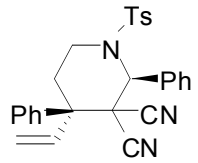
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 4H: arom H), 7.16 (d, 2H, *J* =8.1 Hz: arom H), 6.94 (d, 2H, *J* =8.6 Hz: arom H), 6.12 (dd, 1H, *J* =10.9, 17.2 Hz: CH_2=C**H**), 5.51 (dd, 2H, *J* =10.9, 17.4 Hz: =C**H**$_2$), 4.94 (s, 1H: ArC**H**), 3.95 (m, 1H: C**H**$_2$NTs), 3.77

(m, 1H: C**H**$_2$NTs), 2.40 (s, 3H: C**H**$_3$Ts), 2.31 (s, 3H: C**H**$_3$CO$_2$), 2.29 (m, 1H: C**H**$_2$), 2.03 (m, 1H: C**H**$_2$), 1.42 (s,3H: C**H**$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.10 (O**C**OCH$_3$), δ 151.92 (Quat.), 144.44 (Quat), 133.18 (=**C**H), 136.55 (Quat.), 130.75 (Arom.**C**H), 130.01 (Arom.**C**H), 127.69(Arom.**C**H),130.01 (Arom. **C**H), 120.24 (=**C**H$_2$), 113.78 (**C**N), 113.38 (**C**N), 62.03 (**C**HAr), 50.75 (**C**CN$_2$), 43.42 (Quat.), 41.55 (**C**H$_2$NTs), 31.71 (**C**H$_2$), 25.35 (**C**H$_3$Ts), 21.95, 21.61 (overlapping **C**H$_3$, **C**H$_3$CO$_2$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3056, 2252, 1763, 1599, 1510, 1369, 1163, 814, 760.

HRMS calcd for $C_{25}H_{29}N_4O_4S$ [M+NH_4] 481.1909, found 481.1890.



2,4-diphenyl-1-tosyl-4-vinylpiperidine-3,3-dicarbonitrile

13n (cw2227)

White solid

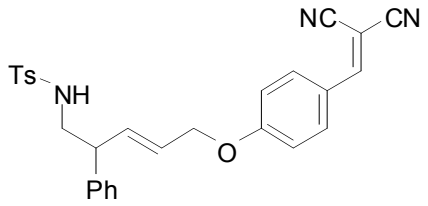
$Pd(PPh_3)_4$: 87% yield, dr =1:>19

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.12 (m, 14H: arom H), 6.45 (dd, *J* =11.1, 17.4 Hz, 1H: CH$_2$=C**H**), 5.72 (dd, 1H, *J* =3.0, 11.1 Hz: =C**H**$_2$), 5.39 (dd, 1H, *J* =2.8, 17.4 Hz: =C**H**$_2$), 4.67 (s, 1H: PhC**H**), 4.26 (m, 1H: C**H**$_2$NTs), 3.61 (m, 1H: C**H**$_2$NTs), 3.01 (app t, 1H: C**H**$_2$), 2.58 (app d, 1H: C**H**$_2$), 2.42 (s, 3H: C**H**$_3$Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.33 (Quat.), 140.58 (Quat), 136.65 (=**C**H), 136.17 (Quat.), 132.49 (Quat.), 130.90-127.97 (Arom.**C**H), 121.89 (=**C**H$_2$), 113.56 (**C**N), 113.26 (**C**N), 65.18 (Ph**C**HNTs), 52.41/50.56 (overlapping **C**CN$_2$, **C**H(Ph)CH=CH$_2$), 43.44 (**C**H$_2$NTs), 30.70 (**C**H$_2$), 21.98 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3094, 3065, 3038, 2253, 1597, 1495, 1350, 1161, 814, 777, 660.

HRMS calcd for $C_{28}H_{25}N_3O_2SNa$ [M+Na] 490.1565, found 490.1560.



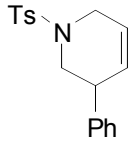
(*E*)-*N*-(5-(4-(2,2-dicyanovinyl)phenoxy)-2-phenylpent-3-enyl)-4-methylbenzenesulfonamide

14g (cw2031)

colorless oil

$Pd(PPh_3)_4$: 90% NMR yield, dr: 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.03-7.95 (m, 26H: arom H), 5.97 (m, 2 H: =C**H**), 5.75 (td, 1H, *J*=15.7, 5.3 Hz: =C**H**CH_2), 5.53 (m, 1H: =C**H**), 5.36 (d, 2H, *J*=5.6 Hz: OC**H**$_2$), 4.62 (d, 2H, *J*=5.6 Hz: OC**H**$_2$), 3.87 (m, 2H: C**H**Ph), 3.51 (br. s., 2H: N**H**Ts), 3.28 (m, 2H: C**H**$_2$NHTs), 3.12 (m, 2H: C**H**$_2$NHTs), 2.46 (s, 3H: C**H**$_3$Ts), 2.43 (s, 3H: C**H**$_3$Ts).



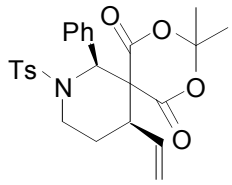
3-phenyl-1-tosyl-1,2,3,6-tetrahydropyridine

15b (cw2048)

White solid

$Pd(PPh_3)_4$: 99% combined yield(**15b**/**15f**)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.70 (d, 2H, *J*=8.1 Hz: arom H), 7.21 - 7.34 (m, 5H: arom H), 7.04 (d, 2H, *J*=8.1 Hz: arom H), 5.68 (m, 1H: =C**H**CH_2), 5.41 (m, 1H: C**H**=), 4.68 (m, 1H: TsNC**H**$_2$), 3.40 (m, 1H: C**H**$_2$CH=), 3.20 (dt, 1H, *J*=12.6, 6.9 Hz: TsNC**H**$_2$), 3.08 (m, 1H: C**H**$_2$CH=), 2.63 (td, 1H, *J*=13.3, 8.3 Hz: C**H**Ph), 2.44 (s, 3H: C**H**$_3$).



(*rac*)-3,3-dimethyl-7-phenyl-8-tosyl-11-vinyl-2,4-dioxa-8-azaspiro[5.5]undecane-1,5-dione

15c (cw2176)

White solid

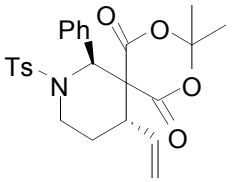
$Pd(PPh_3)_4$: 38% combined yield(**15c**/**15d**), dr: 2:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46 (d, 2H, *J*=8.2Hz: arom H), 7.20 - 7.30 (m, 7H: arom H), 5.50 (m, 1H: C**H**=), 5.12 (dd, 2H, *J*=17.1 Hz: C**H**$_2$=), 4.80 (s, 1H: C**H**Ph), 4.39 (m, 1H: diastereotopic C**H**$_2$NTs), 3.19 (m, 1H: diastereotopic C**H**$_2$NTs), 2.72 (m, 1H: C**H**), 2.44 (s, 3H: C**H**$_3$Ts), 2.35 (m, 1H: diastereotopic C**H**$_2$), 1.81 (ddd, 1H, *J*=13.8, 5.1, 1.7 Hz: diastereotopic C**H**$_2$), 1.50 (s, 3H: C**H**$_3$), 0.71 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 168.6 (O**C**=O), 163.5 (O**C**=O), 144.2 (Quat. Arom.**C**), 136.3 (Quat. Arom.**C**), 135.2 (=**C**H), 134.9 (Quat. Arom.**C**), 130.3 (Arom.**C**H), 129.9 (Arom.**C**H), 129.3 (Arom.**C**H), 128.6 (Arom.**C**H), 128.4 (Arom.**C**H), 120.9 (=**C**H$_2$), 106.8 (**C**(CH$_3$)$_2$), 66.3 (**C**HPh), 61.2 (**C**(CO$_2$R)$_2$), 48.9 (**C**H), 46.4 (**C**H$_2$NTs), 30.1 (**C**H$_3$), 29.1 (**C**H$_3$), 25.8 (**C**H$_2$), 22.0 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2988, 1780, 1749, 1359, 1164, 941.

HRMS calcd for $C_{25}H_{27}NO_6SNa$ [M+Na] 492.1457, found 492.1451.



(*rac*)-3,3-dimethyl-7-phenyl-8-tosyl-11-vinyl-2,4-dioxa-8-azaspiro[5.5]undecane-1,5-dione

15d (cw2176)

White solid

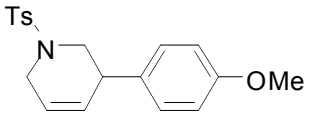
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.33 (m, 5H: arom H), 7.25 (m, 2H: arom H), 7.05 (d, 2H, *J*=8.0 Hz: arom H), 5.68 (dt, 1H, *J*=10.2, 8.6 Hz: C**H**=), 5.59 (s, 1H: C**H**Ph), 5.27 (dd, 1H, *J*=17.2, 0.8 Hz: CH$_2$=C**H**(*E*)), 5.19 (dd, 1H, *J*=10.3, 0.9 Hz: CH$_2$=C**H**(*Z*)), 3.83 (dd, 1H, *J*=5.7 Hz: diastereotopic C**H**$_2$NTs), 3.63 (m, 1H: C**H**), 3.40 (td, 1H, *J*=13.3, 3.7 Hz: diastereotopic C**H**$_2$NTs), 2.33 (s, 3H: C**H**$_3$Ts), 2.72 (m,

1H: diastereotopic C**H**$_2$), 1.90 (s, 3H: C**H**$_3$), 1.83 (m, 1H: diastereotopic C**H**$_2$), 1.66 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.1 (O**C**=O), 164.6 (O**C**=O), 143.2 (Quat. Arom.**C**), 136.3 (=**C**H), 135.8 (Quat. Arom.**C**), 134.9 (Quat. Arom.**C**), 129.9 (Arom.**C**H), 129.5 (Arom.**C**H), 129.1 (Arom.**C**H), 128.6 (Arom.**C**H), 127.4 (Arom.**C**H), 120.5 (=**C**H$_2$), 105.7 (**C**(CH$_3$)$_2$), 61.4 (**C**HPh), 58.5 (**C**(CO$_2$R)$_2$), 39.9 (**C**H$_2$NTs), 38.3 (**C**H), 30.7 (**C**H$_3$), 28.4 (**C**H$_3$), 25.7 (**C**H$_2$), 21.5 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2988, 1780, 1749, 1359, 1164.

HRMS calcd for $C_{25}H_{27}NO_6SNa$ [M+Na] 492.1457, found 492.1451.



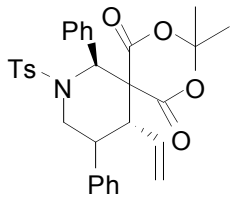
3-(4-methoxyphenyl)-1-tosyl-1,2,3,6-tetrahydropyridine

15e (cw2141)

Colorless oil

$Pd(PPh_3)_4$: 80% combined yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.70 (d, 2H, *J*=8.1 Hz: arom H), 7.35 (d, 2H, *J*=7.6 Hz: arom H), 7.09 (d, 2H, *J*=7.6 Hz: arom H), 6.98 (d, 2H, *J*=8.3 Hz: arom H), 5.65 (dd, 1H, *J*=15.8, 8.0 Hz: =C**H**CH$_2$), 5.04 (dd, 1H, *J*=8.6, 1.8 Hz: C**H**=), 4.64 (m, 1H: TsNC**H**$_2$), 3.79 (s, 3H: OC**H**$_3$), 3.34 (m, 1H: C**H**$_2$CH=), 3.15(dd, 1H, *J*=12.8, 6.2 Hz: TsNC**H**$_2$), 3.10 (m, 1H: C**H**$_2$CH=), 2.68 (m, 1H: C**H**Ph), 2.47 (s, 3H: C**H**$_3$).



(*rac*)-3,3-dimethyl-7,10-diphenyl-8-tosyl-11-vinyl-2,4-dioxa-8-azaspiro[5.5]undecane-1,5-dione

15f (cw2048)

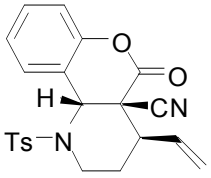
White solid

$Pd(PPh_3)_4$: 99% combined yield(**15b**/**15f**)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46 (dd, 2H, *J*=7.3, 1.0 Hz: arom H), 7.26 (d, 2H, *J*=8.1 Hz: arom H), 7.34 (m, 8H: arom H), 7.00 (ddd, 2H, *J*=7.9, 1.4, 0.7 Hz: arom H), 5.68 (s, 1H: C**H**Ph(NTs)), 5.53 (m, 1H: C**H**=), 5.02 (m, 2H: C**H**$_2$=), 4.09

(m, 1H: C**H**Ph), 3.90 (m, 2H: overlapping diastereotopic C**H**$_2$NTs and C**H**CH=), 3.38 (t, 1H, *J*=13.0 Hz: diastereotopic C**H**$_2$NTs), 2.30 (s, 3H: C**H**$_3$Ts), 1.92 (s, 3H: C**H**$_3$), 1.67 (s, 3H: C**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.5 (O**C**=O), 165.2 (O**C**=O), 143.6 (Quat. Arom.**C**), 140.4 (Quat. Arom.**C**), 136.2 (Quat. Arom.**C**), 135.2 (=**C**H), 135.1 (Quat. Arom.**C**), 130.0 (Arom.**C**H), 129.7 (Arom.**C**H), 129.6 (Arom.**C**H), 129.3 (Arom.**C**H), 129.2 (Arom.**C**H), 128.7 (Arom.**C**H), 127.9 (Arom.**C**H), 127.6 (Arom.**C**H), 123.1 (=**C**H$_2$), 106.3 (**C**(CH$_3$)$_2$), 62.1 (**C**HPh(NTs)), 60.1 (**C**(CO$_2$R)$_2$), 46.6 (**C**H$_2$), 44.0 (**C**HCH=), 42.4 (**C**HPh), 31.2 (**C**H$_3$), 28.8 (**C**H$_3$), 21.8 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.



5-oxo-1-tosyl-4-vinyl-2,3,4,4a,5,10b-hexahydro-1*H*-chromeno[4,3-*b*]pyridine-4a-carbonitrile

16a (cw2169)

colorless oil

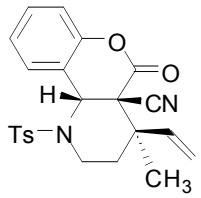
$Pd(PPh_3)_4$: 49% yield, dr = >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3, 2H: arom H), 7.61 (d, *J* = 7.8, 1H: arom H), 7.39 (m, 4H: arom H), 7.16 (d, *J* =8.1, 1H: arom H), 6.12 (s, 1H, *J* =8.3 Hz: TsNC**H**), 5.76 (m, 1H: =C**H**), 5.25(d, 1H, *J* = 10.1 Hz: CH=C**H**(*H*)$_Z$), 5.12 (d, 1H, *J* = 16.9 Hz: CH=C**H**(*H*)$_E$), 3.62 (broad d, 1H, *J* =13.6 Hz: C**H**$_2$NTs), 3.10 (td, 1H, *J* =3.8, 13.6 Hz: C**H**$_2$NTs), 2.48 (m, 4H: overlapping C**H**CH=CH$_2$, C**H**$_3$), 1.63 (m, 2H: C**H**$_2$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3 (O**C**OCH$_3$), 149.6 (Quat.), 145.1 (Quat.), 136.3 (Quat.), 133.8 (=**C**H), 131.4-126.9 (Arom. **C**H), 121.0 (=**C**H$_2$), 117.7 (Arom. **C**H), 115.5 (**C**N), 55.8 (TsN**C**H), 51.5 (**C**CN), 40.7 (**C**HCH=CH$_2$), 39.7 (TsN**C**H$_2$), 27.8 (**C**H$_2$), 22.1 (**C**H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC, NOESY etc. The absolute configuration was assigned, based on the X-ray structure.

FTIR ($CDCl_3$): ν_{max} 3086, 2252, 1772, 1589, 1487, 1354, 1194, 816.

HRMS calcd for $C_{22}H_{20}N_2O_4SNa$ [M+Na] 431.1041, found 431.1032.



4-methyl-5-oxo-1-tosyl-4-vinyl-2,3,4,4a,5,10b-hexahydro-1*H*-chromeno[4,3-*b*]pyridine-4a-carbonitrile

16b (cw2)

colorless oil

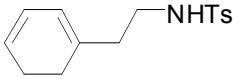
$Pd(PPh_3)_4$: 88% yield, dr = 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-6.98 (14H: arom H), 6.10 (m, 3H: overlapping =C**H**, TsNC**H**), 5.23 (d, 2H, *J* = 10.9 Hz: CH=C**H**(*H*)$_Z$), 5.23 (m, 1H: =C**H**), 5.06 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 4.98 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 4.74 (d, 2H, *J* = 10.9 Hz: CH=C**H**(*H*)$_Z$), 3.69-3.20 (4H: overlapping C**H**$_2$NTs), 2.47 (s, 6H: C**H**$_3$(Ts)), 1.90-1.57 (3H: overlapping C**H**$_2$), 1.39 (4H: overlapping C**H**$_2$, C**H**$_3$), 0.79 (s, 3H: C**H**$_3$(Ts)).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0/160.7 (O**C**OCH$_3$), 149.6 (Quat.), 144.6 (Quat.), 141.0/134.7 (=**C**H), 136.0 (Quat.), 130.8-126.0 (Arom. **C**H), 119.4/119.2 (**C**N), 117.0 (Arom. **C**H), 116.6/116.3 (=**C**H$_2$), 54.9/54.8 (TsN**C**H), 54.0/52.6 (**C**CN), 41.3/40.6 (**C**CH=CH$_2$), 36.6 (TsN**C**H$_2$), 33.5/32.9 (**C**H$_2$), 25.6/19.2 (**C**H$_3$), 21.7 (**C**H$_3$(Ts)). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3092, 3061, 2253, 1761, 1591, 1489, 1331, 1161, 816.

HRMS calcd for $C_{23}H_{26}N_3O_4S$ [M+NH4] 440.1644, found 440.1643.



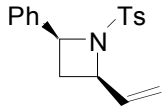
N-(2-(cyclohexa-1,3-dienyl)ethyl)-4-methylbenzenesulfonamide

17b (cw2128)

colorless oil

$Pd(PPh_3)_4$: 89% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (d, 2 H, *J*=8.3 Hz: arom H), 7.32 (d, 2 H, *J*=8.6 Hz: arom H), 5.82 (m, 1 H: =C**H**CH$_2$), 5.65 (d, 1 H, *J*=9.6 Hz: C**H**=), 5.47 (br. s., 1 H: C**H**=C(Quat.)), 4.46 (s, 1 H: N**H**Ts), 3.02 (q, 2 H, *J*=6.1 Hz: C**H**$_2$NHTs), 2.45 (s, 3 H, overlapping C**H**$_2$), 2.16 (t, 3 H, *J*=6.7 Hz: overlapping C**H**$_2$), 2.08 (s, 3 H: C**H**$_3$).



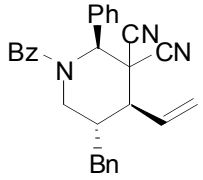
2-phenyl-1-tosyl-4-vinylazetidine

17d (cw2219)

colorless oil

$Pd(PPh_3)_4$: 92% NMR yield yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H: arom H), 7.42 (d, *J* = 7.1 Hz, 2H: arom H) 7.33 (m, 5H: arom H), 6.06 (m, 1H: =C**H**), 5.38 (d, 1H, *J* = 17.2 Hz: CH=C**H**(*H*)$_E$), 5.25 (d, 1H, *J* = 10.4 Hz: CH=C**H**(*H*)$_Z$), 4.81 (t, 1H, *J* =8.3 Hz: PhC**H**), 4.41 (q, *J* =8.1, 4.9 Hz, 1H: C**H**CH=CH_2), 2.61 (d t, *J* =8.3, 10.9 Hz, 1H: C**H**$_2$), 2.45(s, 3H: C**H**$_3$), 1.99(d t, *J* =8.3, 10.9 Hz, 1H: C**H**$_2$). More information about this compound is available in Chapter 2 of this thesis.



1-benzoyl-5-benzyl-2-phenyl-4-vinylpiperidine-3,3-dicarbonitrile

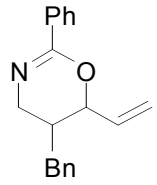
20b (cw2179)

White solid

$Pd(PPh_3)_4$: 36% yield, dr 3.9:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.49 (m, 10H: arom H), 7.18 (t, 3H, *J*=3.1 Hz: arom H), 6.80 (m, 2H, m: arom H), 6.07 (dt, 1H, *J*=16.7, 10.0 Hz: CH_2=C**H**), 5.92 (s, 1H: PhC**H**NBz), 5.70 (d, 1H, *J*=10.2 Hz: CH=C**H**(*E*)), 5.61 (d, 1H, *J*=16.7 Hz: CH=C**H**(*Z*)), 4.03 (dd, 1H, *J*=14.6, 2.9 Hz: C**H**$_2$NTs), 3.59 (dd, 1H, *J*=14.7, 5.1 Hz: C**H**$_2$NTs), 3.38 (dd, 1H, *J*=9.7, 5.7 Hz: C**H**CH=CH_2), 2.79 (d, 1H, *J*=13.4 Hz: diastereotopic C**H**$_2$Ph), 2.53 (m, 2H: overlapping C**H**Bn, diastereotopic C**H**$_2$Ph).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 172.9 (**C**O), 138.9 (Quat. Arom.**C**), 134.6 (Quat. Arom.**C**), 131.4 (Quat. Arom.**C**), 130.4 (=**C**H), 129.9 (Arom.**C**H), 129.7 (Arom.**C**H), 129.4 (Arom.**C**H), 129.3 (Arom.**C**H), 129.0 (Arom.**C**H), 128.1 (Arom.**C**H), 127.7 (Arom.**C**H), 127.0 (Arom.**C**H), 126.9 (Arom.**C**H), 125.7 ((=**C**H_2), 114.9 (**C**N), 114.2 (**C**N), 58.9 (Ph**C**HNTs), 48.4 (**C**HCH=CH_2), 44.1 (**C**H_2NTs), 43.0 (**C**CN_2), 39.1 (Bn**C**H), 35.8 (**C**H_2Ph). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.



5-benzyl-2-phenyl-6-vinyl-5,6-dihydro-4*H*-1,3-oxazine

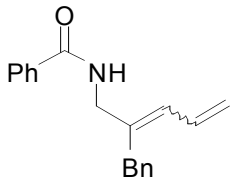
20c (cw2179)

White solid

$Pd(PPh_3)_4$: 39% yield, dr 2.2:1

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ ppm 8.00 (m, 2 H: arom H, overlapping minor/major isomers), 7.44 (m, 3 H: arom H, overlapping minor/major isomers), 7.33 (m, 2 H: arom H, overlapping minor/major isomers), 7.26 (m, 3 H: arom H, overlapping minor/major isomers), 6.00 (m,1 H, overlapping minor/major isomer: C**H**=), 5.40 (m, 2 H: =C**H**$_2$), 4.60 (t, 1 H, *J*=5.9 Hz: OC**H**), 3.59 (dd, 1 H, d, *J*=16.8, 4.9 Hz: C**H**$_2$N), 3.37 (td, 1 H, *J*=16.6, 8.1 Hz: C**H**$_2$N), 2.94 (dd, 1 H, *J*=13.6, 6.3 Hz: C**H**$_2$Ph), 2.58 (m, 1 H: C**H**$_2$Ph), 2.08 (m, 1 H: C**H**Bn).

Minor diastereoisomer: δ ppm 8.00 (m, 2 H: arom H, overlapping minor/major isomers), 7.44 (m, 3 H: arom H, overlapping minor/major isomers), 7.33 (m, 2 H: arom H, overlapping minor/major isomers), 7.26 (m, 3 H: arom H, overlapping minor/major isomers), 6.00 (m,1 H, overlapping minor/major isomer: C**H**=), 5.40 (m, 2 H: =C**H**$_2$), 4.87 (t, 1 H, *J*=3.7 Hz: OC**H**), 3.59 (dd, 1 H, d, *J*=16.8, 4.9 Hz: C**H**$_2$N), 3.37 (td, 1 H, *J*=16.6, 8.1 Hz: C**H**$_2$N), 2.68 - 2.73 (m, 1 H: C**H**$_2$Ph), 2.58 (m, 1 H: C**H**$_2$Ph), 2.43 (m, 1 H: C**H**Bn).



N-(2-benzylpenta-2,4-dienyl)benzamide

20d (cw2186)

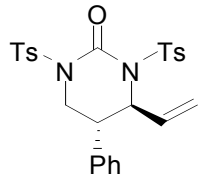
colorless oil

$Pd(PPh_3)_4$: 90% NMR yield, dr =1.7:1

^{1}H NMR (400 MHz, $CDCl_3$) Major diastereoisomer: δ ppm 7.72 (m, 3H: arom H), 7.53 (m, 4H: arom H), 6.98 - 7.19 (m, 3 H: arom H), 6.66 (m, 1H: C**H**=), 6.01 (d, 1H, *J*=11.1 Hz: BnC=C**H**), 5.68 (br. s., 1H: N**H**), 5.15 (m, 2H; =C**H**$_2$), 3.99 (d, 2H, *J*=5.6 Hz: C**H**$_2$NH), 3.42 (s, 2H: C**H**$_2$Ph).

Minor diastereoisomer: δ ppm 7.72 (m, 3H: arom H), 7.53 (m, 4H: arom H), 6.98 - 7.19 (m, 3 H: arom H), 6.77 (m, 1H: C**H**=), 6.14 (d, 1H, *J*=11.1 Hz: BnC=C**H**), 5.68

(br. s., 1H: N**H**), 5.15 (m, 2 H; =C**H**$_2$), 4.18 (d, 2H, *J*=5.6 Hz: C**H**$_2$N), 3.99 (s, 2H: C**H**$_2$Ph).



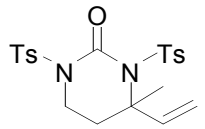
5-phenyl-1,3-ditosyl-4-vinyltetrahydropyrimidin-2(1*H*)-one

21b (cw2104)

colorless oil

$Pd(PPh_3)_4$: 98% yield, dr =3.1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (dd, 2H, *J*=8.4, 2.0 Hz: arom H), 7.77 (d, 2H, *J*=8.3 Hz: arom H), 7.36 (dd, 4H, *J*=8.6, 0.6 Hz: arom H), 7.20 (dd, 4H, *J*=7.6, 0.7 Hz: arom H), 7.12 (d, 2H, *J*=5.0 Hz: arom H), 5.68 (m, 1H: CH_2=C**H**), 5.40 (dd, 2H, *J*=10.6, 1.8 Hz: CH=C**H**(*H*)$_Z$), 5.31 (m, 1H: C**H**NTs), 5.18 (dd, 1H, *J*=17.1, 1.9 Hz: CH=C**H**(*H*)$_E$), 4.35 (dt, 1H, *J*=12.7, 1.9 Hz: diastereotopic C**H**$_2$NTs), 4.07 (dd, 1H, *J*=12.7, 5.3 Hz: diastereotopic C**H**$_2$NTs), 3.53 (m, 1H: PhC**H**.), 2.49 (s, 3H: C**H**$_3$Ts), 2.41 (s, 3H: C**H**$_3$Ts).



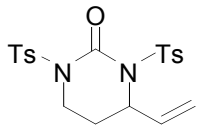
4-methyl-1,3-ditosyl-4-vinyltetrahydropyrimidin-2(1*H*)-one

21e (cw2270)

colorless oil

$Pd(PPh_3)_4$: 72% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (dd, 4H, *J*=14.0, 8.3 Hz: arom H), 7.23 (t, 4H, *J*=9.0 Hz: arom H), 6.13 (dd, 1H, *J*=17.4, 10.8 Hz: CH_2=C**H**), 5.32 (d, 1H, *J*=10.6 Hz: CH=C**H**(*H*)$_Z$), 5.24 (d, 1H, *J*=17.4 Hz: CH=C**H**(*H*)$_E$), 3.89 (dd, 2H, *J*=7.1, 3.9 Hz: C**H**$_2$NTs), 3.83 (d, 2H, *J*=7.8, 4.0 Hz: C**H**$_2$NTs), 2.44 (s, 3H: C**H**$_3$Ts), 2.43 (s, 3H: C**H**$_3$Ts), 2.03 (m, 2H: C**H**$_2$), 1.91 (s, 3H: C**H**$_3$).



1,3-ditosyl-4-vinyltetrahydropyrimidin-2(1*H*)-one

21g (cw2266/267)

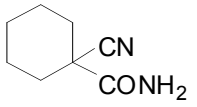
colorless oil

$Pd(PPh_3)_4$: 70% NMR yield

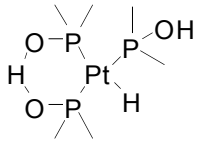
$Pd_2(dba)_3$/Trost ligand: 85% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (m, 4H: arom H), 7.27 (dd, 4H, *J*=5.2, 2.8 Hz: arom H), 5.29 (dd, 1H, *J*=10.5, 1.5 Hz: CH=C**H**$(H)_Z$), 5.25 (m, 1H: C**H**), 5.01 (dd, 1H, *J*=17.1, 1.7 Hz: CH=C**H**$(H)_E$), 4.03 (m, 1H: diastereotopic C**H**$_2$NTs), 3.69 (m, 1H: diastereotopic C**H**$_2$NTs), 2.44 (s, 6H: C**H**$_3$Ts), 2.15 (m, 2H: C**H**$_2$).

^{13}C NMR (125 MHz, $CDCl_3$) δ ppm 157.0 (**C**O), 144.9 (Quat. Arom.**C**), 135.6 (Quat. Arom.**C**), 134.1 (=**C**H), 129.2 (Arom.**C**H), 129.1 (Arom.**C**H), 118.6 (=**C**H$_2$), 56.2 (**C**HCH=CH$_2$), 42.3 (**C**H$_2$NTs), 26.8 (**C**H$_2$), 22.7 (**C**H$_2$NTs).



1-cyanocyclohexanecarboxamide



Cat. **B**

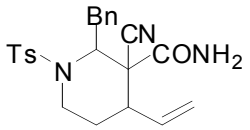
23d (cw3030)

White solid

Cat. **B**: 90% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.42 (br. s., 2H: CON**H**$_2$), 2.03 (m, 2H: C**H**$_2$), 1.82 (m, 5H: C**H**$_2$), 1.62 (m, 2H: C**H**$_2$), 1.26 (m, 1H: C**H**$_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 171.1 (**C**ONH$_2$), 121.1 (**C**N), 46.2 (Quat. **C**), 33.0 (**C**H$_2$), 24.6 (**C**H$_2$), 22.6 (**C**H$_2$).



2-benzyl-3-cyano-1-tosyl-4-vinylpiperidine-3-carboxamide

24d (cw3052)

White solid

Cat. **B**: 95% yield, dr =2.5:1

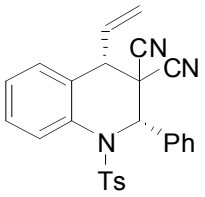
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (m, 7H: arom H), 7.20 (m, 3H: arom H), 7.10 (d, 2H, *J*=8.1 Hz: arom H), 7.02 (d, 2H, *J*=8.0 Hz: arom H), 6.38 (br. s., 1H: CON**H**$_2$), 5.77 (m, 1H: =C**H**), 5.63 (s, 1H: PhC**H**NTs), 5.44 (m, 2H: =C**H**$_2$), 3.52 (dd, 1H, *J*=13.3, 5.1 Hz: diastereotopic C**H**$_2$NTs), 3.24 (dd, 1H, *J*=11.7, 8.7 Hz: diastereotopic C**H**$_2$NTs), 3.11 (dd, 1H, *J*=14.0, 3.4 Hz: diastereotopic C**H**$_2$Ph), 3.00 (t, 1H, *J*=12.6 Hz: C**H**CH=CH$_2$), 2.42 (m, 1H: diastereotopic C**H**$_2$Ph), 2.35 (3, 3H: C**H**$_3$Ts), 2.17 (m, 1H: C**H**Bn).

General procedure for synthesizing starting vinyl benzoxazinanones:

Vinyl benzoxazinanones were prepared as reported in Chapter 2 of this thesis.

General procedure for asymmetric cycloadditions:

In a Schlenk tube under argon, $Pd_2(dba)_3$ (0.05 mmol), Trost ligand (0.11 mmol), vinyl benzoxazinanone **1** (1 mmol) and the benzylidene malononitrile (1 mmol) were dissolved in 5 mL of methylene chloride. The resulting yellow solution was stirred at ambient temperature under Ar until the reaction completion was indicated by TLC (generally 4-6 hrs). Following solvent evaporation under reduced pressure, the crude product was purified via flash chromatography (SiO_2, 5:1 Hexane: Ethyl acetate).



(2*S*,4*S*)-2-phenyl-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33a (cw3194)

white solid

$Pd(PPh_3)_4$: 98% yield, dr = 8.9:1

Pd/Trost ligand: 97% yield, 89% ee (S,S), dr = 19:1

87% yield, 97% ee (S,S), dr = 50:1 after a single recrystallization

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.89 (1 H, dd, *J*=8.0, 1.0 Hz: Ar C*H*), 7.51 - 7.67 (4 H, m: Ar C*H*), 7.39 - 7.51 (5 H, m: Ar C*H*), 7.29 (2 H, d, *J*=7.8 Hz: Ar C*H*), 7.17 (1 H, d, *J*=7.7 Hz: Ar C*H*), 5.91 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.77 (1 H, s: C*H*Ph), 5.61 (1 H, dd, *J*=10.1, 1.0 Hz: CH=C*H*$(H)_{cis}$), 5.09 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.56 (1 H, d, *J*=9.7 Hz: C*H*CH=), 2.47 (3 H, s: CH_3Ts).

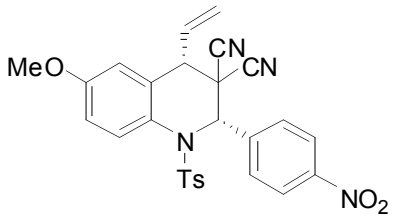
^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.1 (quat. Ar *C*), 136.7 (quat. Ar *C*), 135.1 (quat. Ar *C*), 134.5 (quat. Ar *C*), 131.6 (quat. Ar *C*), 130.2 (Ar *C*H), 130.0 (Ar *C*H), 129.6 (Ar *C*H), 129.3 (*C*H=CH_2), 129.2 (Ar *C*H), 128.6 (Ar *C*H), 128.2 (Ar *C*H), 127.3 (Ar *C*H), 127.0 (Ar *C*H), 126.8 (Ar *C*H), 125.0 (=*C*H_2), 113.9 (*C*N), 111.2

(*C*N), 65.8 (*C*HPh), 50.0 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2986, 2305, 1597, 1483, 1421, 1262, 895.

HRMS calcd for $C_{26}H_{21}N_3O_2SNa$ [M+Na] 462.1252, found 462.1251.

Separated enantiomers on a Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 22.8 min, tr (minor) = 32.1 min.



(2*S*,4*S*)-6-methoxy-2-(4-nitrophenyl)-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33b (cw4155)

white solid

Pd/Trost ligand: 91% yield, 99% ee (S,S), dr = 25:1

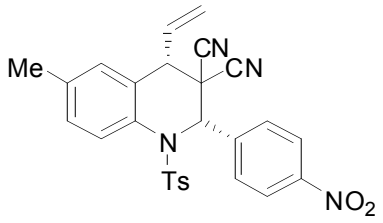
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.89 (1 H, dd, *J*=8.0, 1.0 Hz: Ar C*H*), 7.51 - 7.67 (4 H, m: Ar C*H*), 7.39 - 7.51 (5 H, m: Ar C*H*), 7.29 (2 H, d, *J*=7.8 Hz: Ar C*H*), 7.17 (1 H, d, *J*=7.7 Hz: Ar C*H*), 5.91 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.77 (1 H, s: C*H*Ph), 5.61 (1 H, dd, *J*=10.1, 1.0 Hz: CH=C*H*$(H)_{cis}$), 5.09 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.56 (1 H, d, *J*=9.7 Hz: C*H*CH=), 2.47 (3 H, s: CH_3Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 159.5 (quat. Ar *C*), 148.5 (quat. Ar *C*), 145.5 (quat. Ar *C*), 143.5 (quat. Ar *C*), 133.7 (quat. Ar *C*), 132.8 (quat. Ar *C*), 130.2 (Ar *C*H), 128.7 (*C*H=), 128.3 (Ar *C*H), 127.4 (Ar *C*H), 126.6 (Ar *C*H), 125.6 (=*C*H_2), 124.4 (Ar *C*H), 114.7 (Ar *C*H), 113.4 (*C*N), 113.2 (Ar *C*H), 110.8 (*C*N), 65.1 (*C*HAr), 55.7 (O*C*H_3), 49.1 (*C*HCH=), 48.9 (*C*CN_2), 21.7 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2927, 2303, 1608, 1529, 1350, 1263, 1169, 893.

HRMS calcd for $C_{27}H_{22}N_4O_5SNa$ [M+Na] 537.1209, found 537.1207.

Separated enantiomers on Diacel Chiralpak OD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (minor) = 24.9 min, tr (major) = 28.5 min.



(2*S*,4*S*)-6-methyl-2-(4-nitrophenyl)-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33c (cw4165)

white solid

Pd/Trost ligand: 90% yield, 99% ee (S,S), dr >99:1

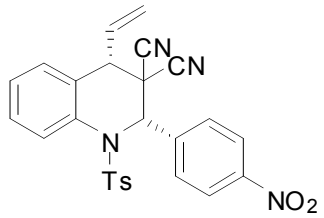
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.31 (2 H, d, *J*=8.7 Hz: Ar C*H*), 7.69 - 7.85 (3 H, m: Ar C*H*), 7.36 - 7.49 (3 H, m: Ar C*H*), 7.29 - 7.36 (2 H, m, *J*=8.0 Hz: Ar C*H*), 6.94 (1 H, s: Ar C*H*), 5.86 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.76 (1 H, s: C*H*Ar), 5.61 (1 H, d, *J*=10.0 Hz: CH=C*H*(H)$_{cis}$), 5.06 (1 H, d, *J*=16.7 Hz: CH=C*H*(H)$_{trans}$), 2.47 (3 H, s: CH_3Ts), 2.38 - 2.45 (4 H, m: overlapping CH_3, C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 148.4 (quat. Ar *C*), 145.4 (quat. Ar *C*), 143.5 (quat. Ar *C*), 138.9 (quat. Ar *C*), 133.8 (quat. Ar *C*), 131.6 (quat. Ar *C*), 131.1 (Ar *C*H), 130.8 (quat. Ar *C*), 130.1 (Ar *C*H), 128.9 (*C*H=CH_2), 128.3 (Ar *C*H), 128.2 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 125.3 (=*C*H_2), 124.4 (Ar *C*H), 113.4 (*C*N), 110.8 (*C*N), 65.0 (*C*HAr), 49.1 (*C*CN_2), 49.0 (*C*HCH=), 21.6 (*C*H_3Ts), 21.4 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2986, 2305, 1528, 1352, 1269, 1259, 895, 818.

HRMS calcd for $C_{27}H_{22}N_4O_4SNa$ [M+Na] 521.1259, found 521.1262.

Separated enantiomers on Diacel Chiralpak OD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (minor) = 16.6 min, tr (major) = 20.1 min.



(2*S*,4*S*)-2-(4-nitrophenyl)-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33d (cw4116)

white solid

Pd/Trost ligand: 78% yield, 96% ee (S,S), dr >99:1

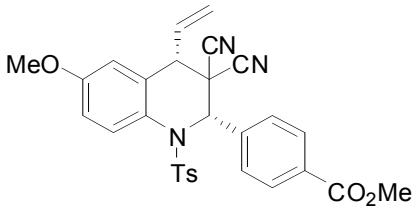
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.32 (2 H, d, *J*=7.5 Hz: Ar C*H*), 7.92 (1 H, d, *J*=8.0 Hz: Ar C*H*), 7.75 (2 H, d, *J*=7.5 Hz: Ar C*H*), 7.60 (1 H, t, *J*=7.7 Hz), 7.42 - 7.47 (1 H, m: Ar C*H*), 7.40 (2 H, d, *J*=7.9 Hz: Ar C*H*), 7.31 (2 H, d, *J*=7.6 Hz: Ar C*H*), 7.17 (1 H, d, *J*=7.6 Hz: Ar C*H*), 5.87 (1 H, ddd, *J*=17.0, 10.0, 9.8 Hz: C*H*=), 5.78 (1 H, s: C*H*Ar), 5.63 (1 H, d, *J*=10.0 Hz: CH=CH_{cis}), 5.09 (1 H, d, *J*=16.7 Hz: CH=CH_{trans}), 2.47 (4 H, s: overlapping CH_3Ts, C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 148.6 (quat. Ar *C*), 145.6 (quat. Ar *C*), 143.4 (quat. Ar *C*), 134.4 (quat. Ar *C*), 133.8 (quat. Ar *C*), 131.1 (quat. Ar *C*), 130.6 (Ar *C*H), 130.2 (Ar *C*H), 128.8 (=*C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.3 (Ar *C*H), 127.3 (Ar *C*H), 126.9 (Ar *C*H), 125.5 (=*C*H_2), 124.5 (Ar *C*H), 113.4 (*C*N), 110.8 (*C*N), 65.1 (*C*HAr), 49.2 (*C*$(CN)_2$), 49.1 (*C*HCH=), 21.7 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2952, 2854, 2337, 1529, 1350, 1327, 1171, 910.

HRMS calcd for $C_{26}H_{20}N_4O_4SNa$ [M+Na] 507.1103, found 507.1097.

Separated enantiomers on Diacel Chiralpak OD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (minor) = 20.6 min, tr (major) = 25.0 min.



methyl 4-((2*S*,4*S*)-3,3-dicyano-6-methoxy-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)benzoate

33e (cw4187)

white solid

Pd/Trost ligand: 99% yield, 92% ee (S,S), dr =25:1

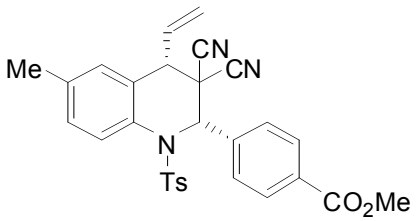
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.11 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.80 (1 H, d, *J*=8.8 Hz: Ar C*H*), 7.62 (2 H, d, *J*=8.4 Hz: Ar C*H*), 7.41 (2 H, d, *J*=8.2 Hz: Ar C*H*), 7.28 - 7.38 (2 H, m, *J*=8.2 Hz: Ar C*H*), 7.06 (1 H, dd, *J*=8.8, 2.7 Hz: Ar C*H*), 6.64 (1 H, d, *J*=2.5 Hz: Ar C*H*), 5.83 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.74 (1 H, s: C*H*Ar), 5.58 (1 H, d, *J*=10.1 Hz: CH=C*H*$(H)_{cis}$), 5.01 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 3.93 (3 H, s: CO_2CH_3), 3.85 (3 H, s: OCH_3), 2.46 (3 H, s: CH_3Ts), 2.36 (1 H, d, *J*=9.6 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 166.3 (CO_2CH_3), 159.4 (quat. Ar *C*), 145.2 (quat. Ar *C*), 141.4 (quat. Ar *C*), 134.1 (quat. Ar *C*), 133.1 (quat. Ar *C*), 131.3 (quat. Ar *C*), 130.5 (Ar *C*H), 130.2 (Ar *C*H), 130.1 (Ar *C*H), 128.9 (*C*H=CH_2), 127.4 (Ar *C*H), 127.1 (Ar *C*H), 127.0 (quat. Ar *C*), 125.4 (=*C*H_2), 114.6 (Ar *C*H), 113.7 (*C*N), 113.1 (Ar *C*H), 111.0 (*C*N), 65.4 (*C*HAr), 55.7 (OCH_3), 52.3 (CO_2CH_3), 49.3 (CCN_2), 49.1 (*C*HCH=), 21.6 (CH_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3055, 2953, 2928, 2305, 1725, 1593, 1495, 1360, 1169, 916.

HRMS calcd for $C_{29}H_{25}N_3O_5SNa$ [M+Na] 550.1413, , found 550.1410.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 31.0 min, tr (minor) = 54.0 min.



methyl 4-((2*S*,4*S*)-3,3-dicyano-6-methyl-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)benzoate

33f (cw4099)

white solid

Pd/Trost ligand: 97% yield, 98% ee (S,S), dr =37:1

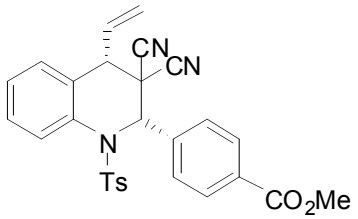
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (2 H, d, *J*=8.4 Hz: Ar C*H*), 7.74 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.60 (2 H, d, *J*=8.4 Hz: Ar C*H*), 7.40 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.35 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.28 (2 H, d, *J*=8.4 Hz: Ar C*H*), 6.92 (1 H, s: Ar C*H*), 5.86 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.75 (1 H, s: C*H*Ar), 5.58 (1 H, d, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 5.04 (1 H, d, *J*=16.7 Hz: CH=C*H*$(H)_{trans}$), 3.91 (3 H, s: CO_2CH_3), 2.44 (4 H, s: overlapping CH_3Ts, C*H*CH=), 2.39 (3 H, s: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 166.3 (CO_2CH_3), 145.2 (quat. Ar *C*), 141.5 (quat. Ar *C*), 138.7 (quat. Ar *C*), 134.2 (quat. Ar *C*), 132.0 (quat. Ar *C*), 131.3 (quat. Ar *C*), 131.1 (quat. Ar *C*), 131.0 (Ar *C*H), 130.5 (Ar *C*H), 130.1 (Ar *C*H), 129.9 (Ar *C*H), 129.2 (*C*H=CH_2), 128.4 (Ar *C*H), 127.3 (Ar *C*H), 127.1 (Ar *C*H), 125.1 (=*C*H_2), 113.8 (*C*N), 111.1 (*C*N), 65.4 (*C*HAr), 52.4 (CO_2CH_3), 49.5 (CCN_2), 49.1 (*C*HCH=),21.6 (CH_3Ts), 21.4 (CH_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2955, 2359, 1722, 1493, 1437, 1366, 1283, 1171, 918

HRMS calcd for $C_{29}H_{29}N_4O_4S$ [M+NH_4] 529.1909, found 529.1904.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 26.5 min, tr (minor) = 38.5 min.



methyl 4-((2*S*,4*S*)-3,3-dicyano-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)benzoate

33g (cw4090)

white solid

Pd/Trost ligand: 76% yield, 96% ee (S,S), dr =25:1

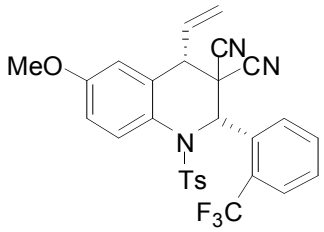
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (2 H, d, *J*=8.46 Hz: Ar C*H*), 7.89 (1 H, d, *J*=7.96 Hz: Ar C*H*), 7.61 (2 H, d, *J*=8.40 Hz: Ar C*H*), 7.56 (1 H, t, *J*=7.77 Hz: Ar C*H*), 7.35 - 7.51 (3 H, m: Ar C*H*), 7.27 (2 H, d, *J*=7.64 Hz: Ar C*H*), 7.14 (1 H, d, *J*=7.64 Hz: Ar C*H*), 5.86 (1 H, dt, *J*=16.75, 9.84 Hz: C*H*=CH_2), 5.77 (1 H, s: C*H*Ar), 5.59 (1 H, d, *J*=10.04 Hz: CH=C*H*(H)$_{cis}$), 5.07 (1 H, d, *J*=16.74 Hz: CH=C*H*(H)$_{trans}$), 3.91 (3 H, s: OCH_3), 2.50 (1 H, d, *J*=9.60 Hz: C*H*CH=), 2.43 (3 H, s: CH_3Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 166.3 (*C*O_2Me), 145.3 (quat. Ar), 141.3 (quat. Ar), 134.8 (quat. Ar *C*), 134.1 (quat. Ar *C*), 131.4 (quat. Ar *C*), 131.3 (quat. Ar *C*), 130.5 (Ar *C*H), 130.4 (Ar *C*H), 130.1 (Ar *C*H), 129.1 (*C*H=CH_2), 128.6 (Ar *C*H), 128.4 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 126.8 (Ar *C*H), 125.3 (=*C*H_2), 113.7 (*C*N), 111.0 (*C*N), 65.4 (*C*HPh), 52.4 (OCH_3), 49.5 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3065, 2953, 2928, 2350, 1724, 1367, 1283, 862.

HRMS calcd for $C_{28}H_{23}N_3O_4SNa$ [M+Na] 520.1307, found 520.1307.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 67.0 min, tr (minor) = 123.6 min.



(2*S*,4*S*)-6-methoxy-1-tosyl-2-(2-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33h (cw4192)

white solid

Pd/Trost ligand: 97% yield, 86% ee (S,S), dr =29:1

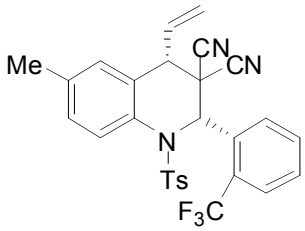
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (2 H, dd, *J*=14.0, 8.2 Hz: Ar C*H*), 7.52 - 7.64 (2 H, m: Ar C*H*), 7.42 - 7.52 (3 H, m: Ar C*H*), 7.35 (2 H, d, *J*=7.8 Hz: Ar C*H*), 7.10 (1 H, dd, *J*=8.8, 2.8 Hz: Ar C*H*), 6.72 (1 H, s: Ar C*H*), 6.30 (1 H, s: C*H*Ar), 5.90 (1 H, ddd, *J*=17.0, 9.8, 9.6 Hz: C*H*=CH_2), 5.61 (1 H, dd, *J*=10.0, 0.6 Hz: CH=C*H*(H)$_{cis}$), 4.99 (1 H, d, *J*=16.7 Hz: CH=C*H*(H)$_{trans}$), 3.89 (3 H, s: OCH_3), 2.49 (3 H, s: CH_3Ts), 2.30 (1 H, d, *J*=9.5 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 159.5 (quat. Ar *C*), 145.2 (quat. Ar *C*), 135.3 (quat. Ar *C*), 134.3 (quat. Ar *C*), 132.9 (quat. Ar *C*), 132.3 (Ar *C*H), 130.5 (Ar *C*H), 130.3 (Ar *C*H), 129.8 (Ar *C*H), 128.9 (*C*H=CH_2), 128.0 (quat. Ar *C*), 127.9 (quat. Ar *C*), 127.7 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 125.5 (=*C*H_2), 114.8 (Ar *C*H), 113.0 (Ar *C*H), 112.6 (*C*N), 111.6 (*C*N), 111.6 (*C*N), 59.8 (*C*HAr), 55.7 (O*C*H_3), 49.9 (*C*HCH=), 49.2 (*C*CN_2), 21.6 (*C*H_3Ts). (Note: *C*F_3 carbon is not found). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2986, 2300, 1495, 1421, 1311, 1271, 895.

HRMS calcd for $C_{28}H_{22}F_3N_3O_3SNa$ [M+Na] 560.1232, found 560.1232.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 16.4 min, tr (minor) = 26.4 min.



(2*S*,4*S*)-6-methyl-1-tosyl-2-(2-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33i (cw4098)

white solid

Pd/Trost ligand: 85% yield, 98% ee (S,S), dr >99:1

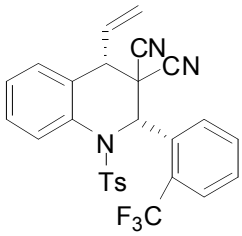
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.68 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.49 - 7.59 (2 H, m: Ar C*H*), 7.41 - 7.47 (3 H, m: Ar C*H*), 7.38 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.32 (2 H, d, *J*=8.5 Hz: Ar C*H*), 6.99 (1 H, s: Ar C*H*), 6.30 (1 H, s: C*H*Ar), 5.91 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.59 (1 H, d, *J*=10.1 Hz: CH=C*H*(H)$_{cis}$), 5.00 (1 H, d, *J*=16.8 Hz: CH=C*H*(H)$_{trans}$), 2.47 (3 H, s: CH_3Ts), 2.44 (3 H, s: CH_3), 2.35 (1 H, d, *J*=9.6 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.1 (quat. Ar *C*), 138.8 (quat. Ar *C*), 135.3 (quat. Ar *C*), 134.5 (quat. Ar *C*), 133.0 (quat. Ar *C*), 132.3 (Ar *C*H), 131.1 (quat. Ar *C*), 131.0 (Ar *C*H), 130.5 (Ar *C*H), 130.2 (Ar *C*H), 129.7 (Ar *C*H), 129.2 (*C*H=CH), 128.8 (Ar *C*H), 128.0 (Ar *C*H), 127.4 (Ar *C*H), 127.2 (Ar *C*H), 125.6 (quat. Ar *C*), 125.2 (=*C*H_2), 112.6 (*C*N), 111.7 (*C*N), 59.8 (*C*HAr), 49.8 (*C*HCH=), 49.4 (*C*CN_2), 21.6 (*C*H_3Ts), 21.5 (*C*H_3). (Note: *C*F_3 carbon is not found). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2925, 2350, 1493, 1310, 1175, 912.

HRMS calcd for $C_{28}H_{26}F_3N_4O_2S$ [M+NH_4] 539.1729, found 539.1719.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (98% Hexane/IPA, 1.0 mL/min), tr (major) = 15.3 min, tr (minor) = 20.9 min.



(2*S*,4*S*)-1-tosyl-2-(2-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33j (cw4097)

white solid

Pd/Trost ligand: 78% yield, 89% ee (S,S), dr =36:1

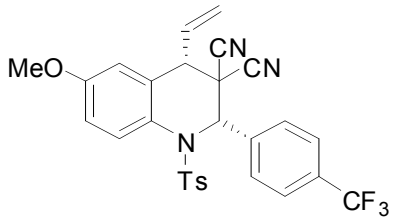
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (1 H, dd, *J*=8.1, 1.0 Hz: Ar C*H*), 7.76 (1 H, d, *J*=7.1 Hz: Ar C*H*), 7.51 - 7.68 (3 H, m: Ar C*H*), 7.43 (4 H, dd, *J*=10.3, 8.0 Hz: Ar C*H*), 7.32 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.20 (1 H, d, *J*=7.7 Hz: Ar C*H*), 6.31 (1 H, s: C*H*Ar), 5.91 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=),5.59 (1 H, d, *J*=10.0 Hz: CH=CH_{cis}), 5.02 (1 H, d, *J*=16.8 Hz: CH=CH_{trans}), 2.46 (3 H, s: CH_3Ts), 2.41 (1 H, d, *J*=9.6 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.3 (quat. Ar *C*), 135.7 (quat. Ar *C*), 135.2 (quat. Ar *C*), 134.4 (quat. Ar *C*), 132.3 (Ar *C*H), 131.4 (quat. Ar *C*), 130.5 (Ar *C*H), 130.4 (Ar *C*H), 130.2 (Ar *C*H), 129.8 (Ar *C*H), 129.0 (=*C*H), 128.5 (Ar *C*H), 127.8 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 127.1 (quat. Ar *C*), 126.9 (Ar *C*H), 125.4 (=*C*H_2), 112.5 (*C*N), 111.6 (*C*N), 59.8 (*C*HAr), 49.9 (*C*HCH=),49.4 (*C*$(CN)_2$), 21.6 (*C*H_3Ts). (Note: *C*F_3 carbon is not found). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2926, 2338, 1599, 1485, 1371, 1312, 1175, 1132, 818.

HRMS calcd for $C_{27}H_{20}F_3N_3O_2SNa$ [M+Na] 530.1126, found 530.1132.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 13.7 min, tr (minor) = 16.9 min.



(2*S*,4*S*)-6-methoxy-1-tosyl-2-(4-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33k (cw4188)

white solid

Pd/Trost ligand: 93% yield, 84% ee (S,S), dr =37:1

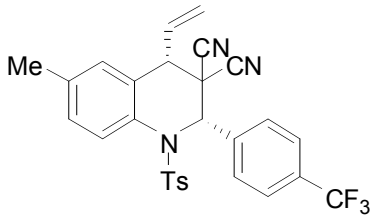
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (2 H, d, *J*=8.8 Hz: Ar C*H*), 7.72 (3 H, t, *J*=8.0 Hz: Ar C*H*), 7.42 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.30 - 7.39 (2 H, m: Ar C*H*), 7.08 (1 H, dd, *J*=8.8, 2.8 Hz: Ar C*H*), 6.67 (1 H, s: Ar C*H*), 5.86 (1 H, dt, *J*=16.7, 9.8 Hz: C*H*=CH_2), 5.74 (1 H, s: C*H*Ar), 5.61 (1 H, d, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 5.04 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 3.87 (3 H, s: OCH_3), 2.48 (3 H, s: CH_3Ts), 2.39 (1 H, d, *J*=9.2 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 159.4 (quat. Ar *C*), 145.3 (quat. Ar *C*), 140.6 (quat. Ar *C*), 133.9 (quat. Ar *C*), 133.0 (quat. Ar *C*), 131.5 (quat. Ar *C*), 130.1 (Ar *C*H), 128.9 (*C*H=CH_2), 127.6 (Ar *C*H), 127.4 (Ar *C*H), 126.9 (quat. Ar *C*), 126.3 (Ar *C*H), 126.2 (Ar *C*H), 125.4 (=*C*H_2), 114.6 (Ar *C*H), 113.6 (*C*N), 113.2 (Ar *C*H), 110.9 (*C*N), 65.3 (*C*HAr), 55.7 (O*C*H_3), 49.2 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts). Note: *C*F_3 carbon is not found. The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3055, 2962, 2928, 2330, 1607, 1495, 1325, 1271, 1171, 914.

HRMS calcd for $C_{28}H_{22}F_3N_3O_3SNa$ [M+Na] 560.1232, , found 560.1231.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 10.0 min, tr (minor) = 18.9 min.



(2*S*,4*S*)-6-methyl-1-tosyl-2-(4-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33l (cw4199)

white solid

Pd/Trost ligand: 88% yield, 86% ee (S,S), dr =56:1

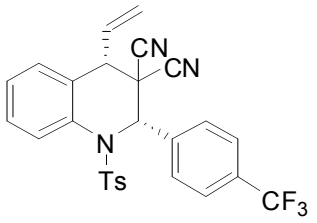
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.60 - 7.73 (4 H, m: Ar C*H*), 7.40 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.36 (1 H, dd, *J*=7.8, 0.9 Hz: Ar C*H*), 7.29 (2 H, d, *J*=8.0 Hz: Ar C*H*), 6.93 (1 H, s: Ar C*H*), 5.87 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.73 (1 H, s: C*H*Ar), 5.60 (1 H, d, *J*=10.1 Hz: CH=C*H*$(H)_{cis}$), 5.05 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.43 - 2.53 (4 H, m: overlapping CH_3Ts, C*H*CH=), 2.40 (3 H, s: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.3 (quat. Ar *C*), 140.7 (quat. Ar *C*), 140.6 (quat. Ar *C*), 138.8 (quat. Ar *C*), 134.1 (quat. Ar *C*), 131.9 (quat. Ar *C*), 131.1 (Ar *C*H), 130.1 (Ar *C*H), 129.8 (quat. Ar *C*), 129.2 (*C*H=CH_2), 128.4 (Ar *C*H), 127.6 (Ar *C*H), 127.4 (Ar *C*H), 127.3 (Ar *C*H), 126.2 (Ar *C*H), 125.2 (=*C*H_2), 113.7 (*C*N), 111.0 (*C*N), 65.3 (*C*HAr), 49.4 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts), 21.4 (*C*H_3). (Note: *C*F_3 carbon is not found). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2925, 2305, 1597, 1493, 1325, 1171, 1132.

HRMS calcd for $C_{28}H_{22}N_3O_2SNa$ [M+Na] 544.1283, found 544.1286.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 13.3 min, tr (minor) = 23.3 min.



(2*S*,4*S*)-1-tosyl-2-(4-(trifluoromethyl)phenyl)-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33m (cw4111)

white solid

Pd/Trost ligand: 90% yield, 91% ee (S,S), dr =45:1

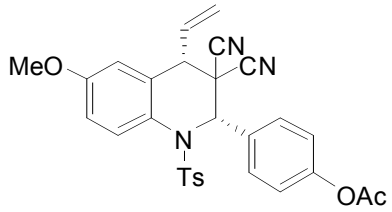
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (1 H, dd, *J*=8.0, 0.9 Hz: Ar C*H*), 7.70 (4 H, q, *J*=8.5 Hz: Ar C*H*), 7.58 (1 H, t, *J*=7.8 Hz: Ar C*H*), 7.37 - 7.50 (3 H, m: Ar C*H*), 7.29 (2 H, d, *J*=8.0 Hz: Ar C*H*), 7.17 (1 H, d, *J*=7.7 Hz: Ar C*H*), 5.89 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=), 5.76 (1 H, s: C*H*Ar), 5.62 (1 H, d, *J*=10.0 Hz: CH=CH_{cis}), 5.10 (1 H, d, *J*=16.8 Hz: CH=CH_{trans}), 2.52 (1 H, d, *J*=9.6 Hz: C*H*CH=), 2.45 (3 H, s: CH_3Ts).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.4 (quat. Ar *C*), 140.5 (quat. Ar *C*), 134.7 (quat. Ar *C*), 134.0 (quat. Ar *C*), 131.3 (quat. Ar *C*), 130.4 (Ar *C*H), 130.1 (Ar *C*H), 129.0 (=*C*H), 128.5 (Ar *C*H), 128.5 (Ar *C*H), 127.7 (Ar *C*H), 127.3 (Ar *C*H), 126.8 (overlapping Ar *C*H, quat. Ar *C*), 126.3 (Ar *C*H), 125.3(=*C*H_2), 113.5 (*C*N), 110.9 (*C*N), 65.3 (*C*HAr), 49.4 (*C*$(CN)_2$), 49.2 (*C*HCH=), 21.6 (*C*H_3Ts). (Note: *C*F_3 carbon is not found). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2927, 2337, 1367, 1327, 1170, 1132, 852.

HRMS calcd for $C_{27}H_{24}F_3N_4O_2S$ [M+NH4] 525.1572, found 525.1586.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (98% Hexane/IPA, 1.0 mL/min), tr (major) = 19.6 min, tr (minor) = 24.2 min.



4-((2*S*,4*S*)-3,3-dicyano-6-methoxy-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)phenyl acetate

33n (cw4185)

white solid

Pd/Trost ligand: 90% yield, 80% ee (S,S), dr =50:1

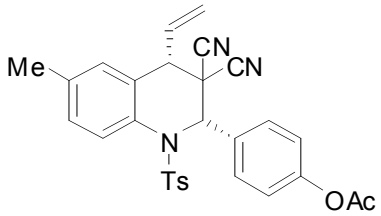
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (1 H, d, *J*=8.8 Hz: Ar C*H*), 7.53 (2 H, d, *J*=8.5 Hz: Ar C*H*), 7.40 (2 H, d, *J*=8.0 Hz: Ar C*H*), 7.30 (2 H, d, *J*=8.0 Hz: Ar C*H*), 7.18 (2 H, d, *J*=8.5 Hz: Ar C*H*), 7.04 (1 H, dd, *J*=8.7, 2.7 Hz: Ar C*H*), 6.65 (1 H, br. s.: Ar C*H*), 5.85 (1 H, dt, *J*=16.8, 9.7 Hz: C*H*=CH_2), 5.71 (1 H, s: C*H*Ar), 5.57 (1 H, d, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 5.01 (1 H, d, *J*=16.7 Hz: CH=C*H*$(H)_{trans}$), 3.85 (3 H, s: OCH_3), 2.46 (3 H, s: CH_3Ts), 2.39 (1 H, d, *J*=9.5 Hz: C*H*CH=), 2.30 (3 H, s: OCOCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.9 (O*C*OCH_3), 159.3 (quat. Ar *C*), 151.5 (quat. Ar *C*), 145.1 (quat. Ar *C*), 134.2 (quat. Ar *C*), 134.1 (quat. Ar *C*), 133.3 (quat. Ar *C*), 130.2 (Ar *C*H), 130.0 (Ar *C*H), 129.1 (*C*H=CH_2), 128.2 (Ar *C*H), 127.4 (Ar *C*H), 127.1 (quat. Ar *C*), 125.2 (=*C*H_2), 122.3 (Ar *C*H), 114.5 (Ar *C*H), 113.9 (*C*N), 113.1 (Ar *C*H), 111.1 (*C*N), 65.3 (*C*HAr), 55.7 (OCH_3), 49.6 (CCN_2), 49.1 (*C*HCH=),21.6 (*C*H_3Ts), 21.2 (OCO*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2928, 2303, 1767, 1607, 1495, 1367, 1263, 1169, 912.

HRMS calcd for $C_{29}H_{29}N_4O_5S$ [M+NH_4] 545.1859, , found 545.1860.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 18.8 min, tr (minor) = 35.6 min.



4-((2*S*,4*S*)-3,3-dicyano-6-methyl-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)phenyl acetate

33o (cw3274)

white solid

Pd/Trost ligand: 73% yield, 90% ee (S,S), dr =70:1

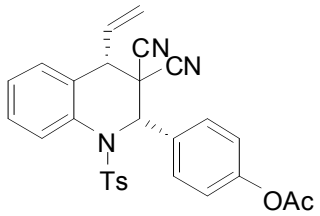
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.68 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.50 (2 H, d, *J*=8.7 Hz: Ar C*H*), 7.38 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.32 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.26 (2 H, d, *J*=8.5 Hz: Ar C*H*), 7.15 (2 H, d, *J*=8.6 Hz: Ar C*H*), 6.91 (1 H, s: Ar C*H*), 5.86 (1 H, dt, *J*=16.8, 9.9 Hz: C*H*=CH_2), 5.71 (1 H, s: C*H*Ar), 5.56 (1 H, d, *J*=10.0 Hz: CH=C*H*(H)$_{cis}$), 5.04 (1 H, d, *J*=16.8 Hz: CH=C*H*(H)$_{trans}$), 2.48 (1 H, d, *J*=9.7 Hz: C*H*CH=), 2.43 (3 H, s: CH_3Ts), 2.38 (3 H, s: CH_3), 2.28 (3 H, s: OCOCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.9 (O*C*OCH$_3$), 151.5 (quat. Ar *C*), 145.1 (quat. Ar *C*), 138.6 (quat. Ar *C*), 134.4 (quat. Ar *C*), 134.1 (quat. Ar *C*), 132.2 (quat. Ar *C*), 131.3 (quat. Ar *C*), 130.9 (Ar *C*H), 130.0 (Ar *C*H), 129.4 (*C*H=CH_2), 128.4 (Ar *C*H), 128.3 (Ar *C*H), 127.4 (Ar *C*H), 124.9 (=*C*H$_2$), 123.0 (Ar *C*H), 122.3 (Ar *C*H), 113.9 (*C*N), 111.2 (*C*N), 65.2 (*C*HAr), 49.8 (*C*CN$_2$), 49.1 (*C*HCH=),21.6 (*C*H$_3$Ts), 21.4 (*C*H$_3$), 21.2 (OCO*C*H$_3$). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2986, 2305, 1769, 1597, 1506, 1493, 1369, 1203, 1171, 914.

HRMS calcd for $C_{29}H_{25}N_3O_4SNa$ [M+Na] 534.1463, found 534.1458.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 28.5 min, tr (minor) = 51.4 min.



4-((2*S*,4*S*)-3,3-dicyano-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)phenyl acetate

33p (cw3268)

white solid

Pd/Trost ligand: 52% yield, 91% ee (S,S), dr =92:1

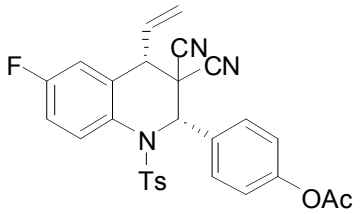
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.52 (1 H, d, *J*=7.8 Hz: Ar C*H*), 7.52 (2 H, d, *J*=8.6 Hz: Ar C*H*), 7.38 - 7.41 (3 H, m: Ar C*H*), 7.28 (2 H, d, *J*=6.1 Hz: Ar C*H*), 7.18 (2 H, d, *J*=8.8 Hz: Ar C*H*), 7.15 (1 H, d, *J*=7.8 Hz: Ar C*H*), 5.87 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.74 (1 H, s: C*H*Ar), 5.58 (1 H, d, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 5.07 (1 H, d, *J*=16.7 Hz: CH=C*H*$(H)_{trans}$), 2.55 (1 H, d, *J*=9.6 Hz: C*H*CH=), 2.42 (3 H, s: CH_3Ts), 2.28 (3 H, s: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.8 (O*C*OMe), 151.5 (quat. Ar *C*), 145.2 (quat. Ar *C*, s), 134.9 (quat. Ar *C*), 134.4 (quat. Ar *C*), 134.0 (quat. Ar *C*), 131.6 (quat. Ar *C*), 130.2 (Ar *C*H), 130.0 (Ar *C*H), 129.2 (*C*H=CH_2), 128.6 (Ar *C*H), 128.5 (Ar *C*H), 128.3 (Ar *C*H), 127.3 (Ar *C*H), 126.8 (Ar *C*H), 125.1 (=*C*H_2), 122.3 (Ar *C*H), 113.8 (*C*N), 111.1 (*C*N), 65.3 (*C*HPh), 49.9 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts), 21.2 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2350, 1769, 1597, 1369, 1204, 1171, 914.

HRMS calcd for $C_{28}H_{27}N_4O_4S$ [M+NH_4] 515.1753, found 515.1752.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 35.4 min, tr (minor) = 76.4 min.



4-((2*S*,4*S*)-3,3-dicyano-6-fluoro-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinolin-2-yl)phenyl acetate

33q (cw4003)

white solid

Pd/Trost ligand: 60% yield, 87% ee (S,S), dr >99:1

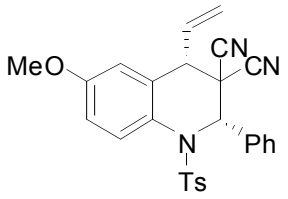
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.74 (1 H, dd, *J*=8.8, 4.8 Hz: Ar C*H*), 7.42 (2 H, d, *J*=8.8 Hz: Ar C*H*), 7.32 (2 H, d, *J*=8.1 Hz: Ar C*H*), 7.22 (2 H, d, *J*=8.3 Hz: Ar C*H*), 7.14 (3 H, m: Ar C*H*), 6.80 (1 H, dd, *J*=8.3, 2.8 Hz: Ar C*H*), 5.82 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.73 (1 H, s: C*H*Ar), 5.61 (1 H, d, *J*=10.1 Hz: CH=C*H*(H)$_{cis}$), 5.08 (1 H, d, *J*=16.8 Hz: CH=C*H*(H)$_{trans}$), 2.50 (1 H, d, *J*=9.5 Hz: C*H*CH=), 2.44 (3 H, s: CH_3Ts), 2.29 (3 H, s: OCOCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.9 (O*C*OCH_3), 165.7 (quat. Ar *C*), 155.3 (quat. Ar *C*), 151.6 (quat. Ar *C*), 145.5 (quat. Ar *C*), 134.1 (quat. Ar *C*), 133.7 (quat. Ar *C*), 132.4 (Ar *C*H), 130.8 (quat. Ar *C*), 130.2 (Ar *C*H), 128.5 (*C*H=CH_2), 128.2 (Ar *C*H), 127.4 (Ar *C*H), 125.8 (=*C*H_2), 122.4 (Ar *C*H), 117.1 (Ar *C*H), 114.2 (Ar *C*H), 113.5 (*C*N), 110.9 (*C*N), 65.3 (*C*HAr), 49.6 (*C*CN_2), 48.9 (*C*HCH=), 21.6 (*C*H_3Ts), 21.2 (OCO*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3062, 2926, 2359, 1713_1487, 1352, 1167, 874.

HRMS calcd for $C_{28}H_{22}FN_3O_4S$ [M+] 515.1315, found 515.1340.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 46.3 min, tr (minor) = 99.7 min.



(2*S*,4*S*)-6-methoxy-2-phenyl-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33r (cw4184)

white solid

Pd/Trost ligand: 92% yield, 86% ee (S,S), dr =54:1

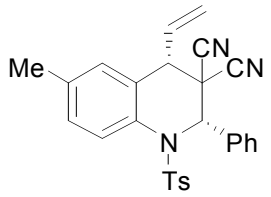
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (1 H, d, *J*=8.8 Hz: Ar C*H*), 7.54 (2 H, d, *J*=7.1 Hz: Ar C*H*), 7.42 (5 H, d, *J*=5.3 Hz: Ar C*H*), 7.30 (1 H, d, *J*=8.2 Hz: Ar C*H*), 7.05 (1 H, dd, *J*=8.8, 2.8 Hz: Ar C*H*), 6.65 (1 H, d, *J*=2.7 Hz: Ar C*H*), 5.85 (1 H, dt, *J*=16.9, 9.8 Hz: C*H*=CH_2), 5.73 (1 H, s: C*H* Ar), 5.57 (1 H, d, *J*=10.1 Hz: CH=C*H*(H)$_{cis}$), 5.01 (1 H, d, *J*=16.8 Hz: CH=C*H*(H)$_{trans}$), 3.84 (3 H, s: OCH_3), 2.46 (3 H, s: CH_3Ts), 2.38 (1 H, d, *J*=9.5 Hz: C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 159.3 (quat. Ar *C*), 145.0 (quat. Ar *C*), 136.8 (quat. Ar *C*), 134.3 (quat. Ar *C*), 133.3 (quat. Ar *C*), 130.2 (Ar *C*H), 130.0 (Ar *C*H), 129.6 (Ar *C*H), 129.2 (overlapping *C*H=CH_2, Ar *C*H), 127.4 (Ar *C*H), 127.3 (quat. Ar *C*), 127.0 (Ar *C*H), 125.1 (=*C*H_2), 114.5 (Ar *C*H), 114.0 (*C*N), 113.0 (Ar *C*H), 111.2 (*C*N), 65.7 (*C*HAr), 55.7 (O*C*H_3), 49.7 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2927, 2320, 1599, 1495, 1364, 1271, 1169, 914.

HRMS calcd for $C_{27}H_{23}N_3O_3SNa$ [M+Na] 492.1358, found 492.1357.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 13.6 min, tr (minor) = 32.3 min.



(2*S*,4*S*)-6-methyl-2-phenyl-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33s (cw3265)

white solid

Pd/Trost ligand: 77% yield, 92% ee (S,S), dr >99:1

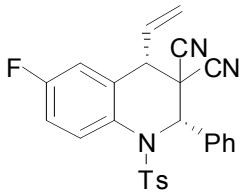
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (1 H, d, *J*=8.1 Hz: Ar C*H*), 7.53 (2 H, dd, *J*=7.7, 1.6 Hz: Ar C*H*), 7.39 - 7.48 (4 H, m: Ar C*H*), 7.35 (1 H, d, *J*=8.0 Hz: Ar C*H*), 7.28 (2 H, d, *J*=8.0 Hz: Ar C*H*), 6.94 (1 H, s: Ar C*H*), 5.89 (1 H, dt, *J*=16.8, 9.9 Hz: C*H*=CH_2), 5.75 (1 H, s: C*H*Ph), 5.58 (1 H, dd, *J*=10.1, 0.9 Hz: CH=C*H*$(H)_{cis}$), 5.05 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.48 (1 H, d, *J*=9.7 Hz: C*H*CH=), 2.45 (3 H, s: CH_3Ts), 2.40 (3 H, s: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 145.0 (quat. Ar *C*), 138.5 (quat. Ar *C*), 136.8 (quat. Ar *C*), 134.6 (quat. Ar *C*), 132.4 (quat. Ar *C*), 131.3 (quat. Ar *C*), 130.9 (Ar *C*H), 130.0 (Ar *C*H), 129.6 (Ar *C*H), 129.4 (*C*H=CH_2), 129.2 (Ar *C*H), 128.5 (Ar *C*H), 127.3 (Ar *C*H), 127.3 (Ar *C*H), 127.0 (Ar *C*H), 124.8 (=*C*H_2), 114.0 (*C*N), 111.3 (*C*N), 65.7 (*C*HAr), 50.0 (*C*CN_2), 49.1 (*C*HCH=), 21.6 (*C*H_3Ts), 21.4 (*C*H_3). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2920, 2302, 1597, 1493, 1366, 1171.

HRMS calcd for $C_{27}H_{23}N_3O_2SNa$ [M+Na] 476.1409, found 476.1408.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (96% Hexane/IPA, 1.0 mL/min), tr (major) = 19.6 min, tr (minor) = 30.3 min.



(2*S*,4*S*)-6-fluoro-2-phenyl-1-tosyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

33t (cw3299)

white solid

Pd/Trost ligand: 75% yield, 87% ee (S,S), dr =87:1

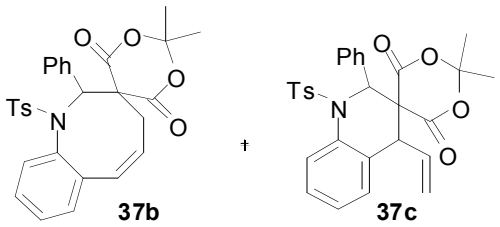
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (1 H, dd, *J*=8.8, 4.9 Hz: Ar C*H*), 7.42 (2 H, dd, *J*=7.8, 1.8 Hz: Ar C*H*), 7.37 (5 H, m: Ar C*H*), 7.23 (2 H, d, *J*=8.1 Hz: Ar C*H*), 7.15 - 7.20 (1 H, m: Ar C*H*), 6.87 (1 H, dd, *J*=8.4, 2.8 Hz: Ar C*H*), 5.83 (1 H, dt, *J*=16.8, 9.8 Hz: C*H*=CH_2), 5.74 (1 H, s: C*H*Ph), 5.61 (1 H, d, *J*=10.1 Hz: CH=C*H*$(H)_{cis}$), 5.06 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.40 - 2.60 (4 H, m: overlapping CH_3Ts, C*H*CH=).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 160.5 (quat. Ar *C*), 145.3 (quat. Ar *C*), 136.4 (quat. Ar *C*), 134.3 (quat. Ar *C*), 131.0 (quat. Ar *C*), 131.0 (quat. Ar *C*), 130.1 (Ar *C*H), 129.7 (Ar *C*H), 129.2 (Ar *C*H), 128.6 (*C*H=), 127.8 (Ar *C*H), 127.3 (Ar *C*H), 126.9 (Ar *C*H), 125.7 ((=*C*H_2), 117.1 (Ar *C*H), 114.4 (Ar *C*H), 113.7 (*C*N), 111.0 (*C*N), 65.8 (*C*HAr), 49.7 (*C*CN_2), 49.0 (*C*HCH=), 21.6 (*C*H_3Ts). The assignments of the ^{1}H and ^{13}C were based on DEPT, COSY, HMQC etc.

FTIR ($CDCl_3$): ν_{max} 3053, 2986, 2305, 1489, 1367, 1271, 914.

HRMS calcd for $C_{26}H_{24}FN_4O_2S$ [M+NH_4] 475.1604, found 475.1600.

Separated enantiomers on Diacel Chiralpak AD-H HPLC column (90% Hexane/IPA, 1.0 mL/min), tr (major) = 14.0 min, tr (minor) = 29.5 min.



37b **37c**

37b:37c=1.5:1

37b:37c=4:1(NMR reaction)

(*Z*)-2',2'-dimethyl-2-phenyl-1-tosyl-2,4-dihydro-1*H*-spiro[benzo[*b*]azocine-3,5'-[1,3]dioxane]-4',6'-dione

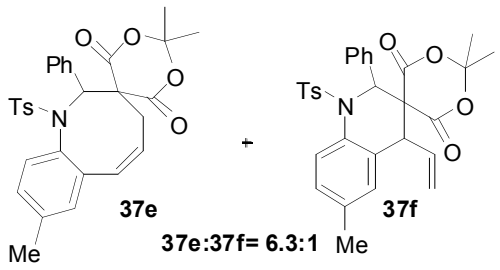
2,2-dimethyl-2'-phenyl-1'-tosyl-4'-vinyl-2',4'-dihydro-1'*H*-spiro[[1,3]dioxane-5,3'-quinoline]-4,6-dione

37b (cw3267)

$Pd(PPh_3)_4$: 63% combined yield

^{1}H NMR (400 MHz, $CDCl_3$) compound **37b:** δ ppm 7.00-7.48 (overlapping Ar C*H*), 6.53 (s, 1H: C*H*Ph), 6.21 (d, 1H, *J*=15.7 Hz: =C*H*), 5.72 (dt, 1H, *J*=15.6, 7.8 Hz: =C*H*CH_2), 2.65 (d, 2H, *J*=7.6 Hz: CH_2), 2.26 (s, 3H: CH_3Ts), 1.65 (s, 3H: CH_3), 1.43 (s, 3H: CH_3).

Compound **37c:** 7.00-7.48 (overlapping Ar C*H*), 6.06 (s, 1H: C*H*Ph), 5.44 (m, 1H: C*H*=CH_2), 4.69 (d, 1H, *J*=15.9 Hz: CH=C*H*$(H)_{trans}$).



37e **37f**

37e:37f= 6.3:1

(*Z*)-2',2',8-trimethyl-2-phenyl-1-tosyl-2,4-dihydro-1*H*-spiro[benzo[*b*]azocine-3,5'-[1,3]dioxane]-4',6'-dione

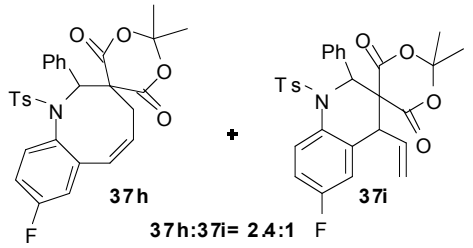
2,2,6'-trimethyl-2'-phenyl-1'-tosyl-4'-vinyl-2',4'-dihydro-1'*H*-spiro[[1,3]dioxane-5,3'-quinoline]-4,6-dione

37e (cw3276)

$Pd(PPh_3)_4$: 85% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) compound **37e:** δ ppm 7.03-7.57 (overlapping Ar C*H*), 6.56 (s, 1H: C*H*Ph), 6.33 (d, 1H, *J*=15.6 Hz: =C*H*), 5.85 (dt, 1H, *J*=15.6, 7.8 Hz: =C*H*CH_2), 2.77 (dd, 2H, *J*=7.6, 1.1 Hz: CH_2), 2.40 (s, 3H: CH_3Ts), 2.28 (s, 3H: CH_3), 1.80 (s, 3H: CH_3), 1.58 (s, 3H: CH_3).

Compound **37f:** 7.03-7.57 (overlapping Ar C*H*), 6.19 (s, 1H: C*H*Ph), 5.59 (dt, 1H, *J*=16.9, 10.1 Hz: C*H*=CH_2), 4.81 (d, 1H, *J*=17.7 Hz: CH=C*H*$(H)_{trans}$).



(*Z*)-8-fluoro-2',2'-dimethyl-2-phenyl-1-tosyl-2,4-dihydro-1*H*-spiro[benzo[*b*]azocine-3,5'-[1,3]dioxane]-4',6'-dione

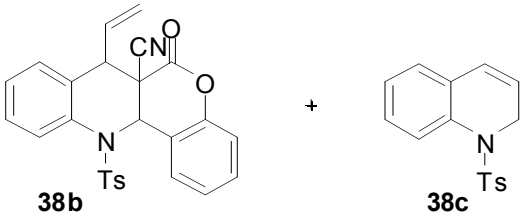
6'-fluoro-2,2-dimethyl-2'-phenyl-1'-tosyl-4'-vinyl-2',4'-dihydro-1'*H*-spiro[[1,3]dioxane-5,3'-quinoline]-4,6-dione

37h (cw4011)

$Pd(PPh_3)_4$: 70% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) compound **37h:** δ ppm 7.06-7.49 (overlapping Ar C*H*), 6.72 (s, 1H: C*H*Ph), 6.34 (d, 1H, *J*=15.6 Hz: =C*H*), 5.88 (t, 1H, *J*=15.7, 7.5 Hz: =C*H*CH_2), 2.76 (d, 2H, *J*=7.8 Hz: CH_2), 2.42 (s, 3H: CH_3Ts), 1.80 (s, 3H: CH_3), 1.60 (s, 3H: CH_3).

Compound **37i:** δ ppm 7.06-7.49 (overlapping Ar C*H*), 6.19 (s, 1H: C*H*Ph), 5.53 (dt, 1H, *J*=16.8, 10.1 Hz: C*H*=CH_2), 5.38 (d, 1H, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 4.84 (d, 1H, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 2.66 (s, 3H: CH_3), 2.43 (s, 3H: CH_3Ts), 1.51 (s, 3H: CH_3).



(higher Conc.of reactants)

6-oxo-12-tosyl-7-vinyl-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-*b*]quinoline-6a-carbonitrile

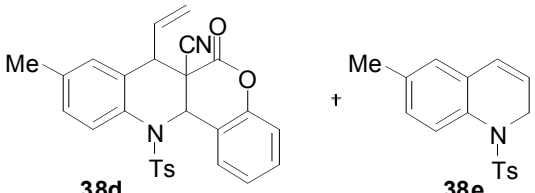
1-tosyl-1,2-dihydroquinoline

38b (cw3256/3260)

$Pd(PPh_3)_4$: 85% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) compound **38b**: δ ppm 7.04-7.34 (overlapping Ar C*H*), 6.34 (s, 1H: C*H*NTs), 5.23 (m, 1H: C*H*=CH_2), 5.16 (d, 1H, *J*=9.8 Hz: CH=C*H*$(H)_{cis}$), 5.05 (d, 1H, *J*=16.4 Hz: CH=C*H*$(H)_{trans}$), 3.47 (d, 1H, *J*=8.8 Hz: C*H*CH=), 2.43 (s, 3H: CH_3Ts).

Compound **38c**: δ ppm 7.04-7.34 (overlapping Ar C*H*), 6.04 (d, 1H, *J*=9.4 Hz: C*H*=), 5.61 (dt, 1H, *J*=9.5, 4.2 Hz: =C*H*CH_2), 5.38 (d, 1H, *J*=10.0 Hz: CH=C*H*$(H)_{cis}$), 4.84 (d, 1H, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 4.43 (dd, 2H, *J*=4.1, 1.7 Hz: CH_2NTs), 2.35 (s, 3H: CH_3Ts).



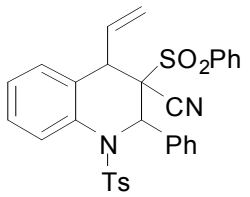
9-methyl-6-oxo-12-tosyl-7-vinyl-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-*b*]quinoline-6a-carbonitrile
6-methyl-1-tosyl-1,2-dihydroquinoline

38d (cw3275)

$Pd(PPh_3)_4$: 80% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) compound **38d**: δ ppm 6.98-7.34 (overlapping Ar C*H*), 6.28 (s, 1H: C*H*NTs), 5.28 (dd, 1 H, *J*=16.4, 9.5 Hz: C*H*=CH_2), 5.17 (d, 1H, *J*=9.9 Hz: CH=C*H*$(H)_{cis}$), 5.03 (d, 1H, *J*=15.9 Hz: CH=C*H*$(H)_{trans}$), 3.36 (d, 1H, *J*=9.2 Hz: C*H*CH=), 2.43 (s, 3H: CH_3Ts), 2.24 (s, 3H: CH_3).

Compound **38e**: δ ppm 6.98-7.34 (overlapping Ar C*H*), 5.99 (1 H, d, *J*=9.3 Hz: =C*H*), 5.57 (1 H, dt, *J*=9.6, 4.17 Hz: =C*H*CH_2), 4.39 (2 H, dd, *J*=4.0, 1.6 Hz: CH_2), 2.35 (3 H, s: overlapping CH_3Ts, CH_3), 2.31 (3 H, s: overlapping CH_3Ts, CH_3).



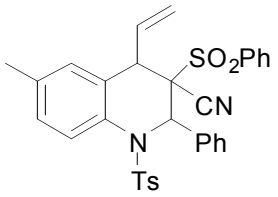
2-phenyl-3-(phenylsulfonyl)-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinoline-3-carbonitrile

39c (cw4046)

white solid

$Pd(PPh_3)_4$:: 80% NMR yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.06-7.76 (overlapping Ar C*H*), 6.07 (s, 1H: C*H*Ph), 5.92 (1H, ddd, *J*=17.0, 10.0, 9.7 Hz: C*H*=CH_2), 5.38 (d, 1H, *J*=10.2 Hz: CH=C*H*$(H)_{cis}$), 4.86(1H, d, *J*=17.2 Hz: CH=C*H*$(H)_{trans}$), 3.18 (1H, d, *J*=9.3 Hz: C*H*CH=), 2.43 (3H, s: CH_3Ts).



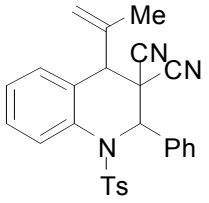
6-methyl-2-phenyl-3-(phenylsulfonyl)-1-tosyl-4-vinyl-1,2,3,4-tetrahydroquinoline-3-carbonitrile

39d (cw4047)

white solid

$Pd(PPh_3)_4$:: 75% yield, dr >19:1

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.99 (2H, d, *J*=8.5 Hz: Ar C*H*), 7.74 (1H, t, *J*=7.5 Hz: Ar C*H*), 7.55 (4H, m: Ar C*H*), 7.46 (1H, d, *J*=8.0 Hz: Ar C*H*), 7.23 (3H, m: Ar C*H*), 7.15 (1H, t, *J*=7.4 Hz: Ar C*H*), 6.99 (3H, d, *J*=7.7 Hz: Ar C*H*), 6.50 (2H, d, *J*=8.1 Hz: Ar C*H*), 5.98 (3 H, m: overlapping C*H*=CH_2, C*H*Ph), 5.38 (dd, 1H, *J*=10.1, 1.4 Hz: CH=C*H*$(H)_{cis}$), 4.79 (1 H, d, *J*=16.8 Hz: CH=C*H*$(H)_{trans}$), 3.12 (1 H, d, *J*=9.3 Hz: C*H*CH=), 2.42 (3 H, s: overlapping CH_3, CH_3Ts), 2.39 (3 H, s: overlapping CH_3, CH_3Ts). The assignments of the ^{1}H was based on COSY.

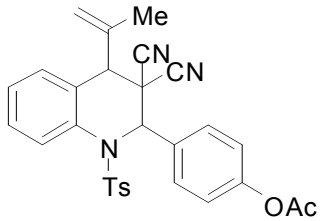


2-phenyl-4-(prop-1-en-2-yl)-1-tosyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

40b (cw3270)

$Pd(PPh_3)_4$: 55% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.12-7.49 (overlapping Ar C*H*), 5.62 (1H, s: Ar C*H*), 5.36 (1 H, s: =CH_2), 5.34 (1 H, s: =CH_2), 2.43 (3H, s: CH_3Ts), 1.74 (3H, s: CH_3).

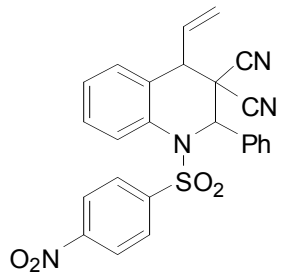


4-(3,3-dicyano-4-(prop-1-en-2-yl)-1-tosyl-1,2,3,4-tetrahydroquinolin-2-yl)phenyl acetate

40c (cw3255)

$Pd(PPh_3)_4$: 67% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.12-7.42 (overlapping Ar C*H*), 5.62 (1H, s: Ar C*H*), 5.36 (1 H, s: =CH_2), 5.34 (1 H, s: =CH_2), 2.35 (6H: overlapping CH_3Ts and CH_3OAc), 1.66 (3H, s: CH_3).

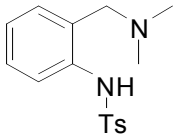


1-(4-nitrophenylsulfonyl)-2-phenyl-4-vinyl-1,2-dihydroquinoline-3,3(4*H*)-dicarbonitrile

41b (cw4055)

$Pd(PPh_3)_4$: 92% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.97-8.26 (overlapping Ar C*H*), 5.95 (1H, ddd, *J*=16.6, 10.0, 9.8 Hz: C*H*=CH_2), 5.86 (1 H, s: C*H*Ph), 5.69 (1 H, d, *J*=10.2 Hz: CH=C*H*$(H)_{cis}$), 5.33 (1H, d, *J*=16.80 Hz: CH=C*H*$(H)_{trans}$), 3.02 (1H, d, *J*=9.5 Hz: C*H*CH=).



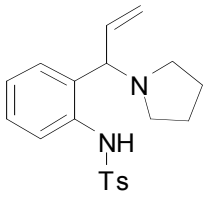
N-(2-((dimethylamino)methyl)phenyl)-4-methylbenzenesulfonamide

42b (cw4180)

$Pd(PPh_3)_4$: 62% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.68 (2H, m d, *J*=8.3 Hz: Ar C*H* (Ts)), 7.54 (1H, d, *J*=7.5 Hz: Ar C*H*), 7.20 - 7.33 (3H, m: overlapping Ar C*H*), 6.98 (2H, dddd, *J*=14.3, 7.5, 6.7, 0.7 Hz: Ar C*H*), 3.12 (2H, s: CH_2), 2.39 (3H, s: CH_3Ts), 2.19 (6H, s: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 143.34 (quat. Ar *C*), 138.00 (quat. Ar *C*), 129.5 (Ar *C*H), 129.5 (Ar *C*H), 128.5 (Ar *C*H), 127.4 (quat. Ar *C*), 126.8 (Ar *C*H), 124.0 (Ar *C*H), 121.3 (Ar *C*H), 63.0 (*C*H_2), 44.5 (*C*H_3), 21.6 (*C*H_3Ts).



4-methyl-*N*-(2-(1-(pyrrolidin-1-yl)allyl)phenyl)benzenesulfonamide

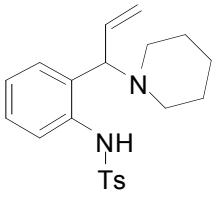
43b (cw3204)

White solid

$Pd(PPh_3)_4$: 97% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 11.89 (1H, br. s.: N*H*Ts), 7.85 (2H, d, *J*=8.1 Hz: arom H), 7.58 (1H, d, *J*=8.1 Hz: arom H), 7.32 (2H, d, *J*=8.0 Hz: arom H), 7.23 (1H, t, *J*=7.7 Hz: arom H), 7.04 (1H, m: arom H), 6.99 (1H, d, *J*=7.3 Hz: arom H), 5.88 (1H, dt, *J*=16.9, 9.5 Hz: C*H*CH=CH_2), 5.14 (1H, d, *J*=16.9 Hz: CH=C*H*(H)$_{trans}$), 5.02 (1H, d, *J*=10.0 Hz: CH=C*H*(H)$_{cis}$), 3.75 (1H, d, *J*=8.9 Hz: C*H*CH=CH_2), 2.61 (2H, m: NCH_2), 2.49 (2H, m: NCH_2), 2.45 (3H, s: CH_3Ts), 1.91 (4H, m: CH_2).

^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 143.4 (quat. Ar *C*), 137.8 (quat. Ar *C*), 137.1 (quat. Ar *C*), 136.5 (*C*H=CH_2), 129.5 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (quat. Ar *C*), 128.2 (Ar *C*H), 127.0 (Ar *C*H), 123.1 (Ar *C*H), 118.1 (Ar *C*H), 117.2 (=*C*H_2), 74.3 (*C*HCH=CH_2), 51.8 (*C*H_2N), 23.6 (*C*H_2), 21.5 (*C*H_3Ts).



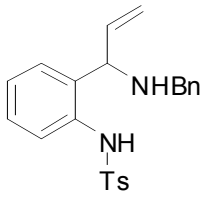
4-methyl-*N*-(2-(1-(piperidin-1-yl)allyl)phenyl)benzenesulfonamide

43b (cw3167)

Colorless oil

$Pd(PPh_3)_4$: 36% yield, 99% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.11 (1H, br. s.: N*H*Ts), 7.72 (2H, d, *J*=8.3 Hz: arom H), 7.42 (1H, dd, *J*=8.1, 1.2 Hz: arom H), 7.21 (2H, d, *J*=8.0 Hz: arom H), 7.13 (1H, td, *J*=7.5, 2.0 Hz: arom H), 6.92 (2H, m: arom H), 5.71 (1H, dt, *J*=16.9, 9.9 Hz: C*H*CH=CH_2), 5.05 (1H, dd, *J*=10.1, 1.6 Hz: CH=C*H*(H)$_{cis}$), 5.00 (1H, dd, *J*=16.9, 1.5 Hz: CH=C*H*(H)$_{trans}$), 3.57 (1H, d, *J*=9.7 Hz: C*H*CH=CH_2), 2.40 (3H, s: CH_2), 2.35 (3H, s: CH_3Ts), 1.62 (5H, br. s.: CH_2), 1.45 (2H, br. s.: CH_2).



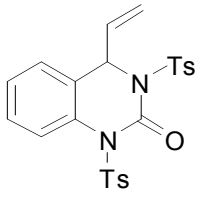
N-(2-(1-(benzylamino)allyl)phenyl)-4-methylbenzenesulfonamide

45c (cw3227)

Colorless oil

$Pd(PPh_3)_4$: 95% NMR yield

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46 (2H, d, *J*=8.3 Hz: arom H), 7.38 (1H, d, *J*=8.2 Hz: arom H), 7.18 (8H, m: arom H), 6.85 (2H, m: arom H), 5.64 (1H, ddd, *J*=17.2, 10.1, 7.4 Hz: C*H*=CH_2), 4.90 (2H, m: =CH_2), 4.00 (1H, d, *J*=7.6 Hz: C*H*CH=CH_2), 3.69 (2H, s: N*H*), 3.52 (2H, m: CH_2), 2.21 (3H, s: CH_3Ts).



1,3-ditosyl-4-vinyl-3,4-dihydroquinazolin-2(1*H*)-one

5c (cw3227)

Colorless oil

$Pd(PPh_3)_4$: 95% NMR yield

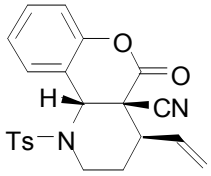
White solid

$Pd(PPh_3)_4$: 55% yield

Pd/Trost ligand: 24% ee

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.94 (2H, d, *J*=8.4 Hz: Ar C*H*), 7.28 (8H, m: Ar C*H*), 5.95 (1H, d, *J*=5.6 Hz: C*H*CH=), 5.83 (1H, td, *J*=11.0, 5.1 Hz: C*H*=CH_2), 5.18 (1H, dd, *J*=10.3, 1.4 Hz: CH=C*H*$(H)_{cis}$), 5.08 (1H, dd, *J*=16.9, 1.5 Hz: CH=C*H*$(H)_{trans}$), 2.46 (6H, s: CH_3Ts).

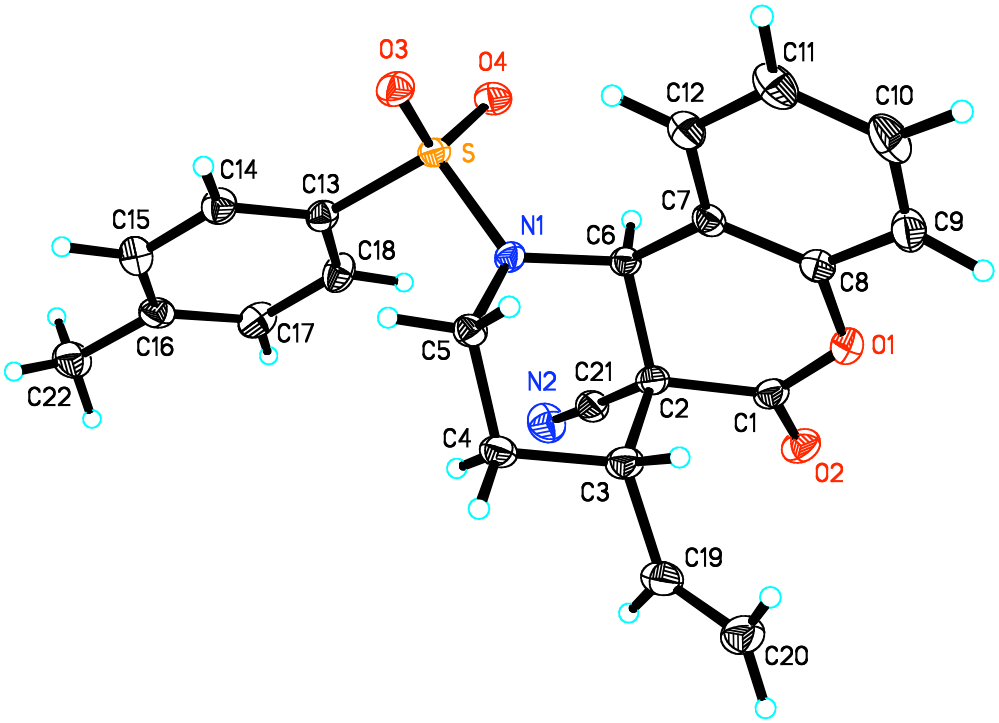
X-ray Crystallography Data for 16a

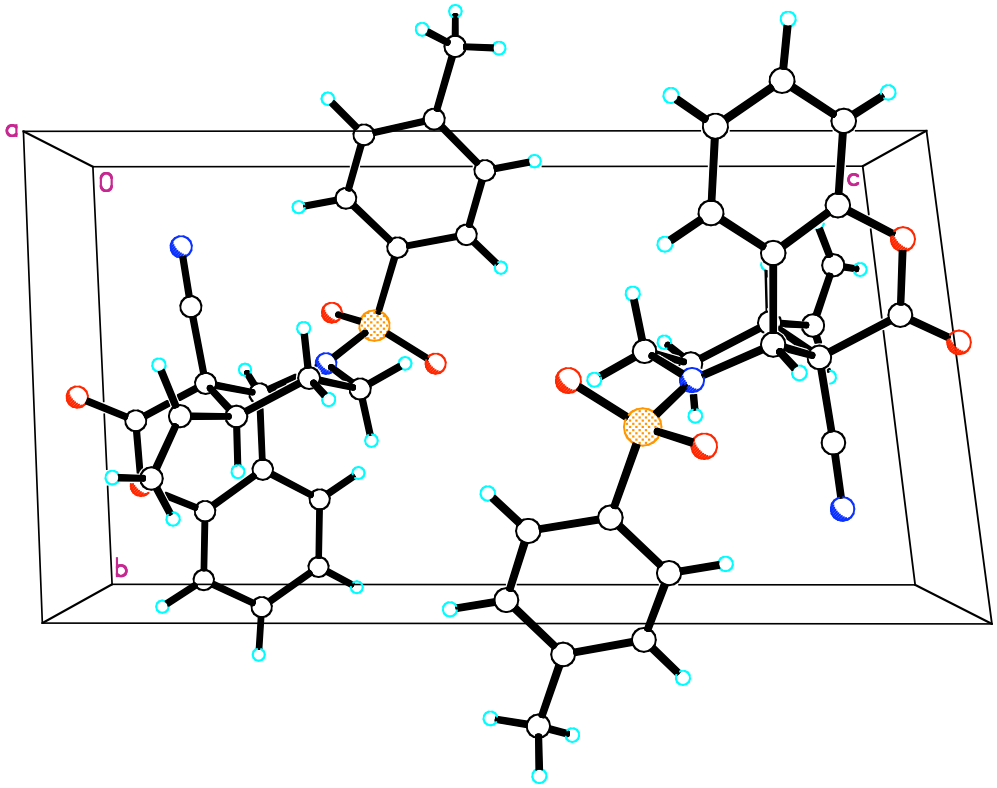


16a (cw2169)

16a was synthesized by the standard decarboxylative olefin insertion reaction from vinyl oxazinanone. The colorless crystal was formed in a solvent mixture of dichloromethane and hexane.

Crystal Structure Data:





Comments The asymmetric unit contains one crystallographically-independent $C_{22}H_{20}N_2O_4S$ molecule. All thermal vibration ellipsoids are drawn at the 50% probability level.

Brief Experimental Description to be Included as Text or as a Footnote at Time of Publication

Colorless crystals of $C_{22}H_{20}N_2O_4S$ are, at 100(2) K, triclinic, space group $P\bar{1}$(C_i^1 – No. 2)[2] with **a** = 7.7457(6) Å, **b** = 8.3807(6) Å, c = 15.163(1) Å, α = 85.166(2)°, β = 89.549(2)°, γ = 74.976(1)°, V = 947.2(1) $Å^3$ and Z = 2 molecules {d_{calcd} = 1.432 g/cm^3; μ_a(MoKα) = 0.204mm^{-1}}. A full hemisphere of diffracted intensities (1850 10-second frames with an ω scan width of 0.30°) was measured for a single-domain specimen using graphite-monochromated MoK_ radiation (λ = 0.71073 Å) on a

Bruker SMART APEX CCD Single Crystal Diffraction System.[3] X-rays were provided by a fine-focus sealed x-ray tube operated at 50kV and 30mA. Lattice constants were determined with the Bruker SAINT software package using peak centers for 5305 reflections. A total of 11612 integrated reflection intensities having $2\theta((MoK\alpha) < 61.00°$ were produced using the Bruker program SAINT;[4] 5684 of these were unique and gave $R_{int} = 0.046$ with a coverage which was 98.5% complete. The data were corrected for variable absorption effects using Gaussian face-indexed absorption corrections; the transmission factors ranged from 0.932 to 0.983. The Bruker software package SHELXTL Version 6.10 was used to solve the structure using "direct methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted using F_o^2 data with the SHELXTL software package.[5] All hydrogen atoms were located from difference Fourier syntheses and included in the structural model as individual isotropic atoms whose parameters were allowed to vary in least-squares refinement cycles.

The final structural model incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. A total of 342 parameters were refined using no restraints, 5684 data and weights of $w = 1/[\sigma^2(F^2) + (0.0790\ P)^2]$, where $P = [F_o^2 + 2F_c^2] / 3$. Final agreement factors at convergence are: R_1(unweighted, based on F) = 0.046 for 4539 independent absorption-corrected reflections having $2\theta(MoK\alpha) < 61.00°$ and $I > 2\sigma(I)$; R_1(unweighted, based on F) = 0.058 and wR_2(weighted, based on F^2) = 0.126 for all 5684 independent absorption-corrected reflections having $2\theta(MoK\alpha) < 61.00°$. The largest shift/s.u. was 0.001 in the final refinement cycle. The final difference map had maxima and minima of 0.79 and -0.51 $e^-/Å^3$, respectively.

Acknowledgment

The authors thank the National Science Foundation (grant CHE-0079282) and the University of Kansas for funds to purchase the X-ray instrument and computers.

Table 1. Crystal data and structure refinement for $C_{22}H_{20}N_2O_4S$.

Empirical formula	$C_{22}H_{20}N_2O_4S$
Formula weight	408.46
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	$P\bar{1}$ (C_i^1 – No. 2)
Unit cell dimensions	**a** = 7.7457(6) Å α = 85.166(2)°.
	b = 8.3807(6) Å _ = 89.549(2)°.
	c = 15.163(1) Å γ = 74.976(1)°.
Volume	947.2(1) Å3
Z	2
Density (calculated)	1.432 Mg/m^3
Absorption coefficient	0.204 mm^{-1}
F(000)	428
Crystal size	0.45 x 0.24 x 0.10 mm^3
Theta range for data collection	2.53° to 30.50°.
Index ranges	$-11 \le h \le 11$, $-11 \le k \le 11$, $-21 \le l \le 21$
Reflections collected	11612
Independent reflections	5684 [R_{int} = 0.046]
Completeness to theta = 30.50°	98.5 %
Absorption correction	Integration
Max. and min. transmission	0.983 and 0.932
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5684 / 0 / 342
Goodness-of-fit on F^2	1.037
Final R indices [I>2sigma(I)]	R_1 = 0.046, wR_2 = 0.119
R indices (all data)	R_1 = 0.058, wR_2 = 0.126
Largest diff. peak and hole	0.79 and -0.51 $e.Å^{-3}$

$R_1 = S ||F_o| - |F_c|| / S |F_o|$

$wR_2 = \{ S [w(F_o^2 - F_c^2)^2] / S [w(F_o^2)^2] \}^{1/2}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for $C_{22}H_{20}N_2O_4S$. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S	-911(1)	3890(1)	3489(1)	15(1)
O(1)	-58(1)	7711(1)	419(1)	23(1)
O(2)	1672(1)	5603(1)	-199(1)	23(1)
O(3)	-1533(1)	4816(1)	4237(1)	20(1)
O(4)	-2197(1)	3546(1)	2910(1)	21(1)
N(1)	337(1)	4818(1)	2869(1)	14(1)
N(2)	2715(2)	2108(2)	1252(1)	27(1)
C(1)	1030(2)	6165(2)	467(1)	19(1)
C(2)	1460(2)	5286(2)	1389(1)	17(1)
C(3)	2895(2)	6035(2)	1820(1)	20(1)
C(4)	3368(2)	5157(2)	2750(1)	19(1)
C(5)	1701(2)	5416(2)	3313(1)	16(1)
C(6)	-226(2)	5539(2)	1975(1)	14(1)
C(7)	-1171(2)	7375(2)	1915(1)	16(1)
C(8)	-1029(2)	8361(2)	1152(1)	19(1)
C(9)	-1879(2)	10035(2)	1038(1)	25(1)
C(10)	-2929(2)	10762(2)	1711(1)	27(1)
C(11)	-3137(2)	9814(2)	2476(1)	25(1)
C(12)	-2249(2)	8134(2)	2581(1)	20(1)
C(13)	622(2)	2035(2)	3892(1)	16(1)
C(14)	1053(2)	1745(2)	4786(1)	20(1)
C(15)	2267(2)	270(2)	5090(1)	22(1)
C(16)	3078(2)	-901(2)	4512(1)	20(1)
C(17)	2638(2)	-563(2)	3614(1)	23(1)
C(18)	1396(2)	880(2)	3299(1)	21(1)
C(19)	4467(2)	6003(2)	1233(1)	24(1)
C(20)	4851(2)	7358(2)	883(1)	28(1)
C(21)	2181(2)	3499(2)	1301(1)	20(1)

C(22)	4369(2)	-2504(2)	4853(1)	27(1)

Table 3. Bond lengths [Å] for $C_{22}H_{20}N_2O_4S$.

S-O(4)	1.4326(10)	C(8)-C(9)	1.384(2)
S-O(3)	1.4369(9)	C(9)-C(10)	1.381(2)
S-N(1)	1.6352(11)	C(9)-H(9)	0.96(2)
S-C(13)	1.7595(14)	C(10)-C(11)	1.382(2)
O(1)-C(1)	1.3463(17)	C(10)-H(10)	0.98(2)
O(1)-C(8)	1.4051(16)	C(11)-C(12)	1.3944(19)
O(2)-C(1)	1.2000(16)	C(11)-H(11)	0.973(18)
N(1)-C(6)	1.4583(16)	C(12)-H(12)	0.941(17)
N(1)-C(5)	1.4705(15)	C(13)-C(14)	1.3851(18)
N(2)-C(21)	1.1400(19)	C(13)-C(18)	1.3940(17)
C(1)-C(2)	1.5211(18)	C(14)-C(15)	1.390(2)
C(2)-C(21)	1.4733(19)	C(14)-H(14)	0.934(16)
C(2)-C(6)	1.5525(17)	C(15)-C(16)	1.3932(19)
C(2)-C(3)	1.5807(18)	C(15)-H(15)	0.968(16)
C(3)-C(19)	1.4993(19)	C(16)-C(17)	1.395(2)
C(3)-C(4)	1.5344(19)	C(16)-C(22)	1.505(2)
C(3)-H(3)	1.02(2)	C(17)-C(18)	1.387(2)
C(4)-C(5)	1.5206(18)	C(17)-H(17)	0.972(18)
C(4)-H(4A)	0.988(16)	C(18)-H(18)	0.941(18)
C(4)-H(4B)	0.922(17)	C(19)-C(20)	1.316(2)
C(5)-H(5A)	0.975(16)	C(19)-H(19)	1.04(2)
C(5)-H(5B)	1.002(16)	C(20)-H(20A)	0.892(13)
C(6)-C(7)	1.5182(18)	C(20)-H(20B)	0.96(2)
C(6)-H(6)	0.915(16)	C(22)-H(22A)	0.91(2)
C(7)-C(8)	1.3843(19)	C(22)-H(22B)	0.90(2)
C(7)-C(12)	1.3937(17)	C(22)-H(22C)	1.01(2)

Table 4. Bond angles [°] for $C_{22}H_{20}N_2O_4S$.

O(4)-S-O(3)	118.87(6)	N(1)-C(5)-H(5A)	107.6(9)
O(4)-S-N(1)	106.60(6)	C(4)-C(5)-H(5A)	112.8(9)
O(3)-S-N(1)	110.07(6)	N(1)-C(5)-H(5B)	108.2(9)
O(4)-S-C(13)	110.21(6)	C(4)-C(5)-H(5B)	111.0(9)
O(3)-S-C(13)	107.32(6)	H(5A)-C(5)-H(5B)	107.8(12)
N(1)-S-C(13)	102.58(6)	N(1)-C(6)-C(7)	114.34(10)
C(1)-O(1)-C(8)	121.81(11)	N(1)-C(6)-C(2)	108.12(10)
C(6)-N(1)-C(5)	117.69(10)	C(7)-C(6)-C(2)	108.54(10)
C(6)-N(1)-S	121.40(8)	N(1)-C(6)-H(6)	106.9(10)
C(5)-N(1)-S	117.72(8)	C(7)-C(6)-H(6)	109.4(10)
O(2)-C(1)-O(1)	119.13(12)	C(2)-C(6)-H(6)	109.4(9)
O(2)-C(1)-C(2)	124.11(13)	C(8)-C(7)-C(12)	117.11(12)
O(1)-C(1)-C(2)	116.62(11)	C(8)-C(7)-C(6)	119.47(11)
C(21)-C(2)-C(1)	108.30(10)	C(12)-C(7)-C(6)	123.37(12)
C(21)-C(2)-C(6)	108.84(11)	C(9)-C(8)-C(7)	122.99(13)
C(1)-C(2)-C(6)	111.77(10)	C(9)-C(8)-O(1)	114.93(12)
C(21)-C(2)-C(3)	111.01(11)	C(7)-C(8)-O(1)	122.04(12)
C(1)-C(2)-C(3)	107.20(11)	C(10)-C(9)-C(8)	118.81(14)
C(6)-C(2)-C(3)	109.71(10)	C(10)-C(9)-H(9)	123.2(12)
C(19)-C(3)-C(4)	114.73(12)	C(8)-C(9)-H(9)	117.9(12)
C(19)-C(3)-C(2)	112.15(11)	C(9)-C(10)-C(11)	120.05(14)
C(4)-C(3)-C(2)	108.34(11)	C(9)-C(10)-H(10)	116.4(11)
C(19)-C(3)-H(3)	92.5(11)	C(11)-C(10)-H(10)	123.5(11)
C(4)-C(3)-H(3)	116.0(11)	C(10)-C(11)-C(12)	120.12(13)
C(2)-C(3)-H(3)	112.6(11)	C(10)-C(11)-H(11)	118.1(12)
C(5)-C(4)-C(3)	110.01(11)	C(12)-C(11)-H(11)	121.8(12)
C(5)-C(4)-H(4A)	112.0(9)	C(7)-C(12)-C(11)	120.89(13)
C(3)-C(4)-H(4A)	106.5(10)	C(7)-C(12)-H(12)	119.6(10)
C(5)-C(4)-H(4B)	108.2(10)	C(11)-C(12)-H(12)	119.5(10)
C(3)-C(4)-H(4B)	112.8(10)	C(14)-C(13)-C(18)	121.02(13)
H(4A)-C(4)-H(4B)	107.4(14)	C(14)-C(13)-S	119.96(10)
N(1)-C(5)-C(4)	109.35(10)	C(18)-C(13)-S	119.02(10)

C(13)-C(14)-C(15)	118.94(12)	C(13)-C(18)-H(18)	122.4(11)
C(13)-C(14)-H(14)	121.9(10)	C(20)-C(19)-C(3)	122.85(15)
C(15)-C(14)-H(14)	119.1(10)	C(20)-C(19)-H(19)	118.5(12)
C(14)-C(15)-C(16)	121.44(13)	C(3)-C(19)-H(19)	118.6(12)
C(14)-C(15)-H(15)	118.1(10)	C(19)-C(20)-H(20A)	112.0(9)
C(16)-C(15)-H(15)	120.4(10)	C(19)-C(20)-H(20B)	121.0(13)
C(15)-C(16)-C(17)	118.28(13)	H(20A)-C(20)-H(20B)	127.0(15)
C(15)-C(16)-C(22)	120.80(13)	N(2)-C(21)-C(2)	178.11(14)
C(17)-C(16)-C(22)	120.90(13)	C(16)-C(22)-H(22A)	110.9(13)
C(18)-C(17)-C(16)	121.32(13)	C(16)-C(22)-H(22B)	110.7(13)
C(18)-C(17)-H(17)	120.0(11)	H(22A)-C(22)-H(22B)	107.7(17)
C(16)-C(17)-H(17)	118.6(11)	C(16)-C(22)-H(22C)	110.2(12)
C(17)-C(18)-C(13)	118.96(13)	H(22A)-C(22)-H(22C)	111.4(17)
C(17)-C(18)-H(18)	118.5(11)	H(22B)-C(22)-H(22C)	105.8(16)

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{22}H_{20}N_2O_4S$. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h2\ a^{*2}U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S	14(1)	15(1)	17(1)	-1(1)	2(1)	-4(1)
O(1)	21(1)	26(1)	19(1)	4(1)	2(1)	-4(1)
O(2)	23(1)	32(1)	17(1)	-3(1)	3(1)	-12(1)
O(3)	20(1)	19(1)	19(1)	-2(1)	5(1)	-2(1)
O(4)	17(1)	23(1)	24(1)	-1(1)	0(1)	-9(1)
N(1)	14(1)	16(1)	14(1)	0(1)	0(1)	-7(1)
N(2)	26(1)	27(1)	25(1)	-5(1)	1(1)	-1(1)
C(1)	16(1)	25(1)	18(1)	0(1)	1(1)	-10(1)
C(2)	14(1)	22(1)	15(1)	-2(1)	1(1)	-6(1)
C(3)	17(1)	26(1)	20(1)	-2(1)	0(1)	-9(1)
C(4)	14(1)	24(1)	20(1)	-2(1)	-1(1)	-5(1)
C(5)	15(1)	20(1)	15(1)	-2(1)	-1(1)	-6(1)

C(6)	13(1)	16(1)	14(1)	-2(1)	0(1)	-4(1)
C(7)	13(1)	16(1)	19(1)	-1(1)	-2(1)	-4(1)
C(8)	14(1)	21(1)	21(1)	1(1)	-1(1)	-5(1)
C(9)	23(1)	22(1)	29(1)	8(1)	-5(1)	-6(1)
C(10)	23(1)	17(1)	38(1)	0(1)	-8(1)	0(1)
C(11)	23(1)	22(1)	28(1)	-7(1)	-4(1)	2(1)
C(12)	18(1)	20(1)	20(1)	-2(1)	-1(1)	-2(1)
C(13)	17(1)	13(1)	18(1)	0(1)	2(1)	-5(1)
C(14)	22(1)	19(1)	18(1)	-3(1)	2(1)	-4(1)
C(15)	23(1)	22(1)	20(1)	0(1)	-3(1)	-5(1)
C(16)	16(1)	16(1)	28(1)	1(1)	1(1)	-5(1)
C(17)	27(1)	15(1)	26(1)	-3(1)	8(1)	-4(1)
C(18)	30(1)	16(1)	18(1)	-1(1)	3(1)	-5(1)
C(19)	17(1)	28(1)	25(1)	-4(1)	2(1)	-5(1)
C(20)	24(1)	36(1)	26(1)	1(1)	-1(1)	-14(1)
C(21)	17(1)	26(1)	16(1)	-2(1)	1(1)	-3(1)
C(22)	22(1)	20(1)	35(1)	4(1)	1(1)	-1(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for $C_{22}H_{20}N_2O_4S$.

	x	y	z	U(eq)
H(3)	2530(30)	7290(30)	1782(13)	41(5)
H(4A)	4280(20)	5630(20)	2998(10)	22(4)
H(4B)	3860(20)	4030(20)	2742(11)	22(4)
H(5A)	1930(20)	4820(20)	3899(10)	18(4)
H(5B)	1190(20)	6620(20)	3395(10)	17(4)
H(6)	-980(20)	4960(20)	1773(10)	14(4)
H(9)	-1660(20)	10650(30)	504(13)	38(5)
H(10)	-3500(30)	11950(30)	1607(13)	40(5)
H(11)	-3900(20)	10360(20)	2936(12)	34(5)
H(12)	-2390(20)	7500(20)	3106(11)	25(4)

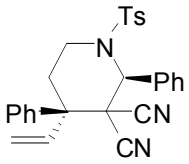
H(14)	570(20)	2520(20)	5189(11)	22(4)
H(15)	2520(20)	60(20)	5719(11)	21(4)
H(17)	3190(20)	-1380(20)	3209(11)	33(5)
H(18)	1180(20)	1080(20)	2685(12)	32(5)
H(19)	5240(30)	4870(30)	1064(14)	46(6)
H(20A)	4111(17)	8273(18)	1064(8)	3(3)
H(20B)	5850(30)	7300(30)	500(13)	42(5)
H(22A)	4850(30)	-2400(30)	5387(14)	42(6)
H(22B)	5280(30)	-2800(30)	4473(13)	41(5)
H(22C)	3760(30)	-3430(30)	4891(13)	40(5)

Table 7. Torsion angles [°] for $C_{22}H_{20}N_2O_4S$.

O(4)-S-N(1)-C(6)	16.46(11)
O(3)-S-N(1)-C(6)	-113.73(10)
C(13)-S-N(1)-C(6)	132.31(10)
O(4)-S-N(1)-C(5)	175.84(9)
O(3)-S-N(1)-C(5)	45.65(11)
C(13)-S-N(1)-C(5)	-68.32(10)
C(8)-O(1)-C(1)-O(2)	171.75(12)
C(8)-O(1)-C(1)-C(2)	-12.31(17)
O(2)-C(1)-C(2)-C(21)	-21.10(17)
O(1)-C(1)-C(2)-C(21)	163.19(11)
O(2)-C(1)-C(2)-C(6)	-140.99(13)
O(1)-C(1)-C(2)-C(6)	43.30(15)
O(2)-C(1)-C(2)-C(3)	98.75(15)
O(1)-C(1)-C(2)-C(3)	-76.96(13)
C(21)-C(2)-C(3)-C(19)	66.25(15)
C(1)-C(2)-C(3)-C(19)	-51.85(15)
C(6)-C(2)-C(3)-C(19)	-173.41(12)
C(21)-C(2)-C(3)-C(4)	-61.40(13)
C(1)-C(2)-C(3)-C(4)	-179.50(10)
C(6)-C(2)-C(3)-C(4)	58.94(14)

C(19)-C(3)-C(4)-C(5)	174.37(12)
C(2)-C(3)-C(4)-C(5)	-59.47(14)
C(6)-N(1)-C(5)-C(4)	-57.25(14)
S-N(1)-C(5)-C(4)	142.60(10)
C(3)-C(4)-C(5)-N(1)	56.64(14)
C(5)-N(1)-C(6)-C(7)	-64.72(13)
S-N(1)-C(6)-C(7)	94.65(12)
C(5)-N(1)-C(6)-C(2)	56.29(13)
S-N(1)-C(6)-C(2)	-144.33(9)
C(21)-C(2)-C(6)-N(1)	66.62(13)
C(1)-C(2)-C(6)-N(1)	-173.81(10)
C(3)-C(2)-C(6)-N(1)	-55.03(13)
C(21)-C(2)-C(6)-C(7)	-168.83(10)
C(1)-C(2)-C(6)-C(7)	-49.26(13)
C(3)-C(2)-C(6)-C(7)	69.52(13)
N(1)-C(6)-C(7)-C(8)	149.76(11)
C(2)-C(6)-C(7)-C(8)	28.98(15)
N(1)-C(6)-C(7)-C(12)	-32.74(17)
C(2)-C(6)-C(7)-C(12)	-153.52(12)
C(12)-C(7)-C(8)-C(9)	1.0(2)
C(6)-C(7)-C(8)-C(9)	178.64(12)
C(12)-C(7)-C(8)-O(1)	-176.55(11)
C(6)-C(7)-C(8)-O(1)	1.10(19)
C(1)-O(1)-C(8)-C(9)	170.98(12)
C(1)-O(1)-C(8)-C(7)	-11.29(19)
C(7)-C(8)-C(9)-C(10)	-0.5(2)
O(1)-C(8)-C(9)-C(10)	177.17(12)
C(8)-C(9)-C(10)-C(11)	-0.9(2)
C(9)-C(10)-C(11)-C(12)	1.8(2)
C(8)-C(7)-C(12)-C(11)	-0.1(2)
C(6)-C(7)-C(12)-C(11)	-177.63(12)
C(10)-C(11)-C(12)-C(7)	-1.3(2)
O(4)-S-C(13)-C(14)	-133.00(11)
O(3)-S-C(13)-C(14)	-2.17(13)

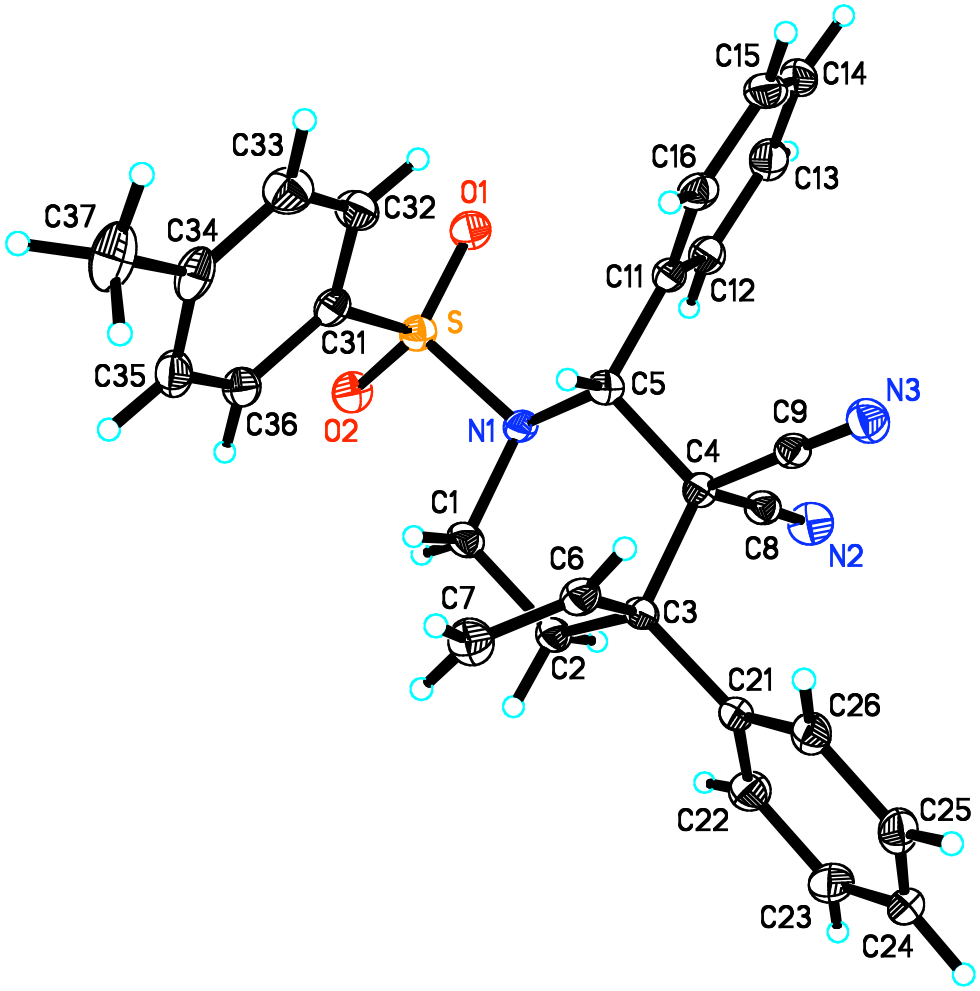
N(1)-S-C(13)-C(14)	113.80(11)
O(4)-S-C(13)-C(18)	47.45(12)
O(3)-S-C(13)-C(18)	178.27(10)
N(1)-S-C(13)-C(18)	-65.76(11)
C(18)-C(13)-C(14)-C(15)	-0.5(2)
S-C(13)-C(14)-C(15)	179.98(10)
C(13)-C(14)-C(15)-C(16)	1.2(2)
C(14)-C(15)-C(16)-C(17)	-0.2(2)
C(14)-C(15)-C(16)-C(22)	-179.04(13)
C(15)-C(16)-C(17)-C(18)	-1.5(2)
C(22)-C(16)-C(17)-C(18)	177.37(13)
C(16)-C(17)-C(18)-C(13)	2.1(2)
C(14)-C(13)-C(18)-C(17)	-1.1(2)
S-C(13)-C(18)-C(17)	178.41(10)
C(4)-C(3)-C(19)-C(20)	-121.00(16)
C(2)-C(3)-C(19)-C(20)	114.83(16)
C(1)-C(2)-C(21)-N(2)	-142(5)
C(6)-C(2)-C(21)-N(2)	-20(5)
C(3)-C(2)-C(21)-N(2)	101(5)

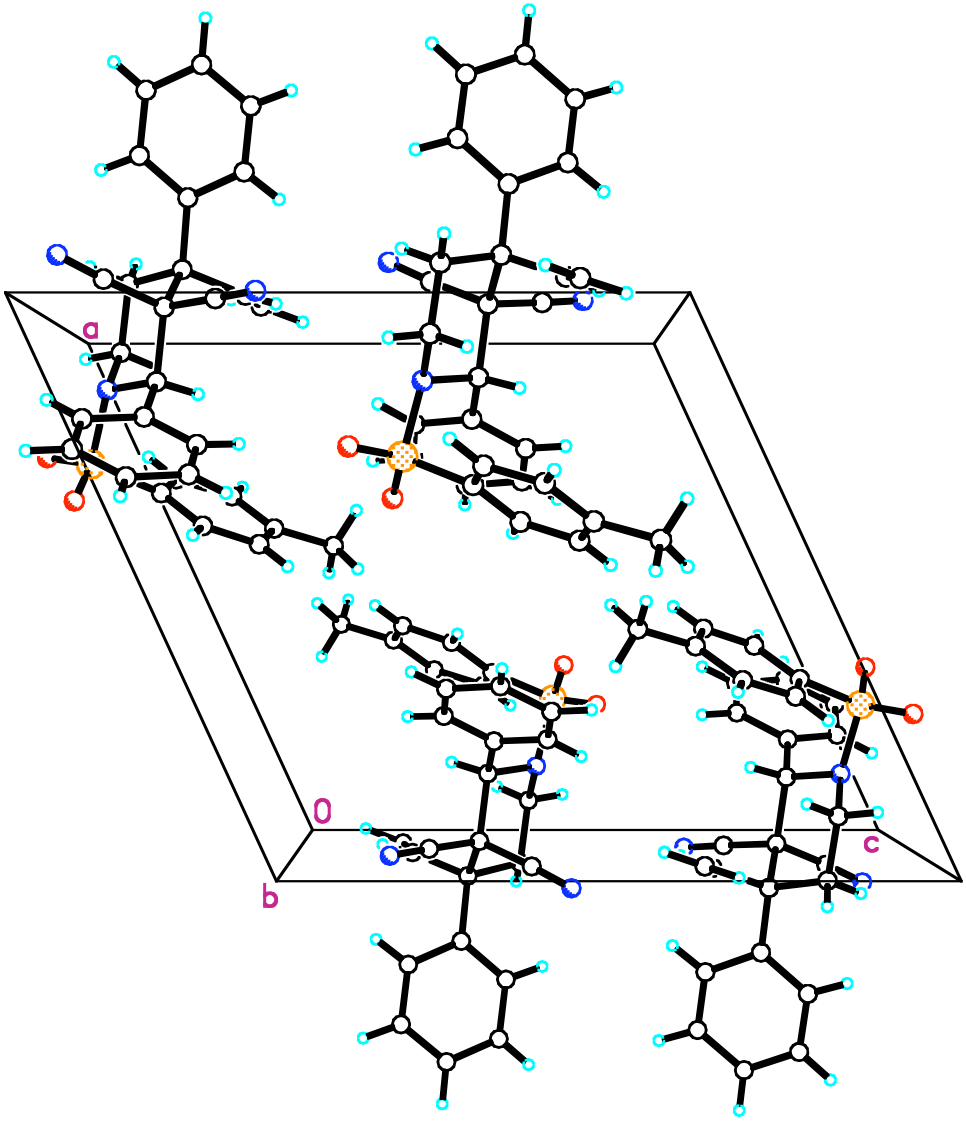


13n (cw2227)

13n was synthesized by the standard decarboxylative olefin insertion reaction from vinyl oxazinanone. The colorless crystal was formed in a solvent mixture of dichloromethane and hexane.

Crystal Structure Data:





Comments

The asymmetric unit contains one crystallographically-independent $C_{28}H_{25}N_3O_2S$ molecule. All thermal vibration ellipsoids are drawn at the 50% probability level.

Brief Experimental Description to be Included as Text or as a Footnote at Time of Publication

Colorless crystals of $C_{28}H_{25}N_3O_2S$ are, at 100(2) K, monoclinic, space group $P2_1/c$ – C_{2h}^5 (No. 14)[2] with **a** = 12.781(1) Å, **b** = 14.997(1) Å, **c** = 13.507(1) Å, **β** = 114.749(1)°, V = 2351.1(2) Å^3 and Z = 4 molecules {d_{calcd} = 1.321 g/cm^3; μ_a(MoKα) = 0.169 mm^{-1}}. A full hemisphere of diffracted intensities (1850 10-second frames with an ω scan width of 0.30°) was measured for a single-domain specimen using graphite-monochromated MoK_ radiation (λ = 0.71073 Å) on a Bruker SMART APEX CCD Single Crystal Diffraction System.[3] X-rays were provided by a fine-focus sealed x-ray tube operated at 50kV and 30mA. Lattice constants were determined with the Bruker SAINT software package using peak centers for 3098 reflections. A total of 28640 integrated reflection intensities having 2θ((MoKα)< 61.07° were produced using the Bruker program SAINT;[4] 7181 of these were unique and gave R_{int} = 0.069 with a coverage which was 99.8% complete. The data were corrected empirically for variable absorption effects using 893 equivalent reflections; the relative transmission factors ranged from 0.951 to 1.000. The Bruker software package SHELXTL Version 6.10 was used to solve the structure using "direct methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted using F_o^2 data with the SHELXTL software package.[5] All hydrogen atoms were located from difference Fourier syntheses and included in the structural model as individual isotropic atoms whose parameters were allowed to vary in least-squares refinement cycles.

The final structural model incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. A total of 407 parameters were refined using no restraints, 7181 data and weights of $w = 1/[\sigma^2(F^2) + (0.0302\ P)^2]$, where $P = [F_o^2 + 2F_c^2] / 3$. Final agreement factors at convergence are: R_1(unweighted, based on F) = 0.049 for 4498 independent absorption-corrected reflections having 2θ(MoKα)< 61.07° and I>2σ(I); R_1(unweighted, based on F) = 0.086 and wR_2(weighted, based on F^2) = 0.091 for all 7181 independent absorption-corrected reflections having 2θ(MoKα)< 61.07°. The

largest shift/s.u. was 0.000 in the final refinement cycle. The final difference map had maxima and minima of 0.46 and -0.46 $e^-/Å^3$, respectively.

Table 1. Crystal Data and Structure Refinement for $C_{28}H_{25}N_3O_2S$.

Empirical formula	$C_{28}H_{25}N_3O_2S$	
Formula weight	467.57	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c - C_{2h}^5$ (No. 14)	
Unit cell dimensions	**a** = 12.7805(7) Å	α = 90.000°
	b = 14.9966(9) Å	_ = 114.749(1)°
	c = 13.5072(8) Å	γ = 90.000°
Volume	2351.1(2) $Å^3$	
Z	4	
Density (calculated)	1.321 Mg/m^3	
Absorption coefficient	0.169 mm^{-1}	
F(000)	984	
Crystal size	0.28 x 0.24 x 0.08 mm^3	
Theta range for data collection	2.72° to 30.54°	
Index ranges	$-18 \le h \le 18$, $-21 \le k \le 21$, $-19 \le l \le 19$	
Reflections collected	28640	
Independent reflections	7181 [R_{int} = 0.069]	
Completeness to theta = 30.54°	99.8 %	
Absorption correction	Empirical	
Max. and min. transmission	0.728 and 0.692	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7181 / 0 / 407	
Goodness-of-fit on F^2	0.852	
Final R indices [I>2sigma(I)]	R_1 = 0.049, wR_2 = 0.083	
R indices (all data)	R_1 = 0.086, wR_2 = 0.091	
Largest diff. peak and hole	0.459 and -0.464 $e^-/Å^3$	

$R_1 = ||F_o| - |F_c|| / |F_o|$

$wR_2 = \{ [w(F_o^2 - F_c^2)^2] / [w(F_o^2)^2] \}^{1/2}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for $C_{28}H_{25}N_3O_2S$. U (eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
S	2742(1)	1008(1)	5313(1)	18(1)
O(1)	3440(1)	1777(1)	5758(1)	22(1)
O(2)	2597(1)	369(1)	6034(1)	22(1)
N(1)	1399(1)	1345(1)	4486(1)	16(1)
N(2)	-869(1)	3066(1)	4150(1)	26(1)
N(3)	-206(1)	3343(1)	1382(1)	23(1)
C(1)	650(1)	539(1)	4065(1)	19(1)
C(2)	-598(1)	779(1)	3421(1)	18(1)
C(3)	-801(1)	1371(1)	2434(1)	15(1)
C(4)	-28(1)	2226(1)	2940(1)	15(1)
C(5)	1294(1)	1981(1)	3607(1)	16(1)
C(6)	-374(1)	953(1)	1641(1)	18(1)
C(7)	-257(2)	100(1)	1501(2)	25(1)
C(8)	-481(1)	2700(1)	3644(1)	18(1)
C(9)	-119(1)	2860(1)	2062(1)	16(1)
C(11)	1982(1)	2836(1)	3983(1)	17(1)
C(12)	2045(1)	3302(1)	4898(1)	20(1)
C(13)	2616(1)	4111(1)	5173(2)	24(1)
C(14)	3117(1)	4469(1)	4530(2)	25(1)
C(15)	3050(1)	4021(1)	3617(1)	24(1)
C(16)	2493(1)	3201(1)	3347(1)	20(1)
C(21)	-2079(1)	1627(1)	1817(1)	17(1)
C(22)	-2862(2)	1516(1)	2275(2)	24(1)

C(23)	-4019(2)	1715(1)	1691(2)	29(1)
C(24)	-4426(2)	2027(1)	637(2)	26(1)
C(25)	-3662(2)	2145(1)	168(2)	24(1)
C(26)	-2503(1)	1944(1)	746(1)	20(1)
C(31)	3253(1)	450(1)	4459(1)	17(1)
C(32)	3877(2)	911(1)	4004(1)	23(1)
C(33)	4207(2)	480(1)	3271(2)	27(1)
C(34)	3896(1)	-395(1)	2963(1)	24(1)
C(35)	3271(2)	-850(1)	3436(1)	24(1)
C(36)	2961(1)	-443(1)	4190(1)	21(1)
C(37)	4219(2)	-854(2)	2144(2)	34(1)

Table 3. Bond lengths [Å] for $C_{28}H_{25}N_3O_2S$.

S-O(1)	1.4280(11)	C(4)-C(5)	1.589(2)
S-O(2)	1.4326(11)	C(5)-C(11)	1.517(2)
S-N(1)	1.6866(13)	C(5)-H(5)	0.975(15)
S-C(31)	1.7563(16)	C(6)-C(7)	1.312(2)
N(1)-C(5)	1.4838(19)	C(6)-H(6)	0.938(16)
N(1)-C(1)	1.499(2)	C(7)-H(7A)	0.994(17)
N(2)-C(8)	1.1404(19)	C(7)-H(7B)	0.995(17)
N(3)-C(9)	1.1391(19)	C(11)-C(16)	1.391(2)
C(1)-C(2)	1.506(2)	C(11)-C(12)	1.392(2)
C(1)-H(1A)	0.966(16)	C(12)-C(13)	1.385(2)
C(1)-H(1B)	0.954(16)	C(12)-H(12)	0.941(15)
C(2)-C(3)	1.531(2)	C(13)-C(14)	1.384(2)
C(2)-H(2A)	0.973(16)	C(13)-H(13)	0.978(16)
C(2)-H(2B)	0.952(15)	C(14)-C(15)	1.376(2)
C(3)-C(6)	1.526(2)	C(14)-H(14)	0.912(17)
C(3)-C(21)	1.539(2)	C(15)-C(16)	1.391(2)
C(3)-C(4)	1.588(2)	C(15)-H(15)	0.924(16)
C(4)-C(8)	1.485(2)	C(16)-H(16)	0.953(16)
C(4)-C(9)	1.486(2)	C(21)-C(22)	1.390(2)

C(21)-C(26)	1.399(2)	C(32)-C(33)	1.387(2)
C(22)-C(23)	1.386(2)	C(32)-H(32)	0.922(16)
C(22)-H(22)	0.947(16)	C(33)-C(34)	1.383(2)
C(23)-C(24)	1.377(3)	C(33)-H(33)	0.925(17)
C(23)-H(23)	0.933(17)	C(34)-C(35)	1.393(2)
C(24)-C(25)	1.381(2)	C(34)-C(37)	1.501(2)
C(24)-H(24)	0.963(16)	C(35)-C(36)	1.380(2)
C(25)-C(26)	1.388(2)	C(35)-H(35)	0.945(17)
C(25)-H(25)	0.956(17)	C(36)-H(36)	0.968(16)
C(26)-H(26)	0.951(15)	C(37)-H(37A)	0.990(19)
C(31)-C(32)	1.380(2)	C(37)-H(37B)	0.997(19)
C(31)-C(36)	1.396(2)	C(37)-H(37C)	0.98(2)

Table 4. Bond angles [°] for $C_{28}H_{25}N_3O_2S$.

O(1)-S-O(2)	119.31(7)	C(3)-C(2)-H(2A)	108.1(9)
O(1)-S-N(1)	108.61(6)	C(1)-C(2)-H(2B)	108.5(9)
O(2)-S-N(1)	105.37(7)	C(3)-C(2)-H(2B)	109.8(9)
O(1)-S-C(31)	108.86(7)	H(2A)-C(2)-H(2B)	107.8(13)
O(2)-S-C(31)	108.53(7)	C(6)-C(3)-C(2)	113.13(13)
N(1)-S-C(31)	105.26(7)	C(6)-C(3)-C(21)	109.44(12)
C(5)-N(1)-C(1)	112.65(12)	C(2)-C(3)-C(21)	111.76(13)
C(5)-N(1)-S	116.68(10)	C(6)-C(3)-C(4)	107.01(12)
C(1)-N(1)-S	108.69(10)	C(2)-C(3)-C(4)	104.18(12)
N(1)-C(1)-C(2)	112.31(13)	C(21)-C(3)-C(4)	111.13(12)
N(1)-C(1)-H(1A)	111.5(10)	C(8)-C(4)-C(9)	106.43(13)
C(2)-C(1)-H(1A)	109.2(10)	C(8)-C(4)-C(3)	108.83(12)
N(1)-C(1)-H(1B)	104.4(10)	C(9)-C(4)-C(3)	110.23(12)
C(2)-C(1)-H(1B)	110.5(10)	C(8)-C(4)-C(5)	110.78(12)
H(1A)-C(1)-H(1B)	108.9(13)	C(9)-C(4)-C(5)	108.08(12)
C(1)-C(2)-C(3)	113.20(14)	C(3)-C(4)-C(5)	112.33(12)
C(1)-C(2)-H(2A)	109.3(9)	N(1)-C(5)-C(11)	115.41(13)

N(1)-C(5)-C(4)	108.73(12)	C(23)-C(22)-C(21)	121.12(17)
C(11)-C(5)-C(4)	108.88(12)	C(23)-C(22)-H(22)	117.2(10)
N(1)-C(5)-H(5)	110.3(9)	C(21)-C(22)-H(22)	121.6(10)
C(11)-C(5)-H(5)	109.1(9)	C(24)-C(23)-C(22)	120.81(18)
C(4)-C(5)-H(5)	103.7(9)	C(24)-C(23)-H(23)	117.9(11)
C(7)-C(6)-C(3)	126.76(17)	C(22)-C(23)-H(23)	121.3(11)
C(7)-C(6)-H(6)	117.2(10)	C(23)-C(24)-C(25)	119.00(17)
C(3)-C(6)-H(6)	116.1(10)	C(23)-C(24)-H(24)	119.2(10)
C(6)-C(7)-H(7A)	120.8(10)	C(25)-C(24)-H(24)	121.8(10)
C(6)-C(7)-H(7B)	119.2(10)	C(24)-C(25)-C(26)	120.52(17)
H(7A)-C(7)-H(7B)	120.0(14)	C(24)-C(25)-H(25)	122.2(10)
N(2)-C(8)-C(4)	177.36(17)	C(26)-C(25)-H(25)	117.2(10)
N(3)-C(9)-C(4)	178.99(17)	C(25)-C(26)-C(21)	121.04(17)
C(16)-C(11)-C(12)	118.89(15)	C(25)-C(26)-H(26)	119.1(9)
C(16)-C(11)-C(5)	118.79(15)	C(21)-C(26)-H(26)	119.8(9)
C(12)-C(11)-C(5)	122.13(15)	C(32)-C(31)-C(36)	120.34(16)
C(13)-C(12)-C(11)	120.40(17)	C(32)-C(31)-S	119.82(13)
C(13)-C(12)-H(12)	120.5(10)	C(36)-C(31)-S	119.72(13)
C(11)-C(12)-H(12)	119.1(10)	C(31)-C(32)-C(33)	119.38(17)
C(14)-C(13)-C(12)	120.14(17)	C(31)-C(32)-H(32)	119.7(10)
C(14)-C(13)-H(13)	122.5(10)	C(33)-C(32)-H(32)	120.9(10)
C(12)-C(13)-H(13)	117.3(10)	C(34)-C(33)-C(32)	121.40(17)
C(15)-C(14)-C(13)	120.11(17)	C(34)-C(33)-H(33)	118.9(11)
C(15)-C(14)-H(14)	119.6(11)	C(32)-C(33)-H(33)	119.6(11)
C(13)-C(14)-H(14)	120.2(11)	C(33)-C(34)-C(35)	118.36(16)
C(14)-C(15)-C(16)	119.96(17)	C(33)-C(34)-C(37)	121.60(17)
C(14)-C(15)-H(15)	121.5(10)	C(35)-C(34)-C(37)	120.04(17)
C(16)-C(15)-H(15)	118.5(10)	C(36)-C(35)-C(34)	121.21(17)
C(15)-C(16)-C(11)	120.48(17)	C(36)-C(35)-H(35)	120.9(10)
C(15)-C(16)-H(16)	119.8(9)	C(34)-C(35)-H(35)	117.9(10)
C(11)-C(16)-H(16)	119.8(9)	C(35)-C(36)-C(31)	119.25(16)
C(22)-C(21)-C(26)	117.52(15)	C(35)-C(36)-H(36)	119.1(9)
C(22)-C(21)-C(3)	121.86(14)	C(31)-C(36)-H(36)	121.6(9)
C(26)-C(21)-C(3)	120.56(14)	C(34)-C(37)-H(37A)	108.1(11)

C(34)-C(37)-H(37B)	113.0(11)	H(37A)-C(37)-H(37C)	109.8(16)
H(37A)-C(37)-H(37B)	106.3(15)	H(37B)-C(37)-H(37C)	107.8(16)
C(34)-C(37)-H(37C)	111.6(12)		

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{28}H_{25}N_3O_2S$. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h2\ a^{*2}U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S	16(1)	20(1)	14(1)	1(1)	4(1)	0(1)
O(1)	20(1)	23(1)	18(1)	-3(1)	1(1)	-2(1)
O(2)	23(1)	26(1)	15(1)	7(1)	6(1)	1(1)
N(1)	13(1)	18(1)	14(1)	3(1)	2(1)	-1(1)
N(2)	26(1)	29(1)	24(1)	-3(1)	12(1)	-1(1)
N(3)	25(1)	21(1)	21(1)	1(1)	8(1)	-1(1)
C(1)	20(1)	17(1)	19(1)	4(1)	5(1)	-2(1)
C(2)	17(1)	16(1)	18(1)	3(1)	6(1)	-1(1)
C(3)	15(1)	14(1)	16(1)	0(1)	6(1)	-2(1)
C(4)	16(1)	16(1)	13(1)	1(1)	5(1)	0(1)
C(5)	16(1)	18(1)	14(1)	0(1)	6(1)	-1(1)
C(6)	16(1)	20(1)	17(1)	-1(1)	5(1)	0(1)
C(7)	27(1)	24(1)	22(1)	-1(1)	8(1)	0(1)
C(8)	17(1)	18(1)	16(1)	1(1)	5(1)	-2(1)
C(9)	15(1)	16(1)	16(1)	-4(1)	5(1)	-1(1)
C(11)	14(1)	16(1)	16(1)	2(1)	3(1)	0(1)
C(12)	19(1)	21(1)	17(1)	2(1)	5(1)	1(1)
C(13)	22(1)	22(1)	23(1)	-3(1)	3(1)	0(1)
C(14)	19(1)	17(1)	29(1)	2(1)	0(1)	-3(1)
C(15)	16(1)	26(1)	24(1)	8(1)	4(1)	-4(1)
C(16)	16(1)	24(1)	16(1)	2(1)	4(1)	-1(1)
C(21)	15(1)	14(1)	19(1)	-1(1)	5(1)	-1(1)
C(22)	22(1)	25(1)	26(1)	6(1)	10(1)	-2(1)

C(23)	18(1)	29(1)	42(1)	7(1)	15(1)	-2(1)
C(24)	15(1)	18(1)	36(1)	1(1)	3(1)	1(1)
C(25)	25(1)	20(1)	19(1)	-2(1)	1(1)	2(1)
C(26)	22(1)	18(1)	19(1)	-3(1)	7(1)	1(1)
C(31)	15(1)	21(1)	14(1)	1(1)	4(1)	2(1)
C(32)	23(1)	21(1)	25(1)	-1(1)	9(1)	-3(1)
C(33)	27(1)	31(1)	26(1)	4(1)	16(1)	0(1)
C(34)	23(1)	29(1)	16(1)	3(1)	4(1)	10(1)
C(35)	23(1)	19(1)	24(1)	0(1)	5(1)	4(1)
C(36)	19(1)	20(1)	23(1)	4(1)	8(1)	1(1)
C(37)	38(1)	39(1)	25(1)	2(1)	13(1)	16(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{28}H_{25}N_3O_2S$.

	x	y	z	U(eq)
H(1A)	905(14)	173(11)	3619(13)	25(5)
H(1B)	747(14)	213(10)	4704(13)	22(5)
H(2A)	-879(13)	1095(10)	3891(13)	22(5)
H(2B)	-1031(13)	243(10)	3189(12)	16(4)
H(5)	1501(13)	1690(10)	3069(13)	18(4)
H(6)	-176(13)	1352(10)	1212(13)	19(5)
H(7A)	-426(14)	-354(11)	1950(14)	31(5)
H(7B)	23(15)	-92(11)	948(14)	35(5)
H(12)	1694(13)	3059(10)	5327(13)	20(5)
H(13)	2661(14)	4402(11)	5838(14)	26(5)
H(14)	3459(15)	5017(11)	4689(14)	28(5)
H(15)	3378(14)	4248(11)	3177(13)	24(5)
H(16)	2466(13)	2885(10)	2725(13)	19(4)
H(22)	-2632(13)	1294(10)	2993(13)	18(4)

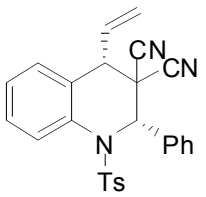
H(23)	-4549(15)	1633(11)	1994(14)	33(5)
H(24)	-5235(14)	2154(10)	246(13)	24(5)
H(25)	-3902(14)	2352(11)	-564(14)	28(5)
H(26)	-1995(13)	2015(10)	400(12)	16(4)
H(32)	4056(14)	1502(11)	4179(13)	22(5)
H(33)	4624(15)	787(11)	2963(14)	33(5)
H(35)	3078(14)	-1452(11)	3236(14)	28(5)
H(36)	2528(13)	-779(10)	4504(13)	22(5)
H(37A)	4661(16)	-427(13)	1908(15)	42(6)
H(37B)	4731(16)	-1379(12)	2451(15)	39(6)
H(37C)	3536(18)	-1058(13)	1510(18)	59(7)

Table 7. Torsion angles [°] for $C_{28}H_{25}N_3O_2S$.

O(1)-S-N(1)-C(5)	54.31(12)
O(2)-S-N(1)-C(5)	-176.76(11)
C(31)-S-N(1)-C(5)	-62.14(12)
O(1)-S-N(1)-C(1)	-177.01(10)
O(2)-S-N(1)-C(1)	-48.09(12)
C(31)-S-N(1)-C(1)	66.53(12)
C(5)-N(1)-C(1)-C(2)	-55.70(18)
S-N(1)-C(1)-C(2)	173.41(12)
N(1)-C(1)-C(2)-C(3)	58.95(19)
C(1)-C(2)-C(3)-C(6)	57.68(18)
C(1)-C(2)-C(3)-C(21)	-178.25(13)
C(1)-C(2)-C(3)-C(4)	-58.17(17)
C(6)-C(3)-C(4)-C(8)	175.03(12)
C(2)-C(3)-C(4)-C(8)	-64.91(15)
C(21)-C(3)-C(4)-C(8)	55.60(16)
C(6)-C(3)-C(4)-C(9)	58.66(16)
C(2)-C(3)-C(4)-C(9)	178.72(13)
C(21)-C(3)-C(4)-C(9)	-60.77(16)
C(6)-C(3)-C(4)-C(5)	-61.93(15)

C(2)-C(3)-C(4)-C(5)	58.13(16)
C(21)-C(3)-C(4)-C(5)	178.64(12)
C(1)-N(1)-C(5)-C(11)	176.90(13)
S-N(1)-C(5)-C(11)	-56.36(16)
C(1)-N(1)-C(5)-C(4)	54.25(16)
S-N(1)-C(5)-C(4)	-179.00(10)
C(8)-C(4)-C(5)-N(1)	63.94(16)
C(9)-C(4)-C(5)-N(1)	-179.82(12)
C(3)-C(4)-C(5)-N(1)	-58.00(16)
C(8)-C(4)-C(5)-C(11)	-62.56(16)
C(9)-C(4)-C(5)-C(11)	53.68(16)
C(3)-C(4)-C(5)-C(11)	175.50(12)
C(2)-C(3)-C(6)-C(7)	25.8(2)
C(21)-C(3)-C(6)-C(7)	-99.52(19)
C(4)-C(3)-C(6)-C(7)	139.97(17)
C(9)-C(4)-C(8)-N(2)	62(4)
C(3)-C(4)-C(8)-N(2)	-57(4)
C(5)-C(4)-C(8)-N(2)	179(100)
C(8)-C(4)-C(9)-N(3)	-76(10)
C(3)-C(4)-C(9)-N(3)	42(10)
C(5)-C(4)-C(9)-N(3)	165(10)
N(1)-C(5)-C(11)-C(16)	142.92(14)
C(4)-C(5)-C(11)-C(16)	-94.52(17)
N(1)-C(5)-C(11)-C(12)	-42.1(2)
C(4)-C(5)-C(11)-C(12)	80.51(18)
C(16)-C(11)-C(12)-C(13)	-0.6(2)
C(5)-C(11)-C(12)-C(13)	-175.58(15)
C(11)-C(12)-C(13)-C(14)	0.8(2)
C(12)-C(13)-C(14)-C(15)	-0.1(3)
C(13)-C(14)-C(15)-C(16)	-0.9(3)
C(14)-C(15)-C(16)-C(11)	1.2(2)
C(12)-C(11)-C(16)-C(15)	-0.5(2)
C(5)-C(11)-C(16)-C(15)	174.74(14)
C(6)-C(3)-C(21)-C(22)	141.14(16)

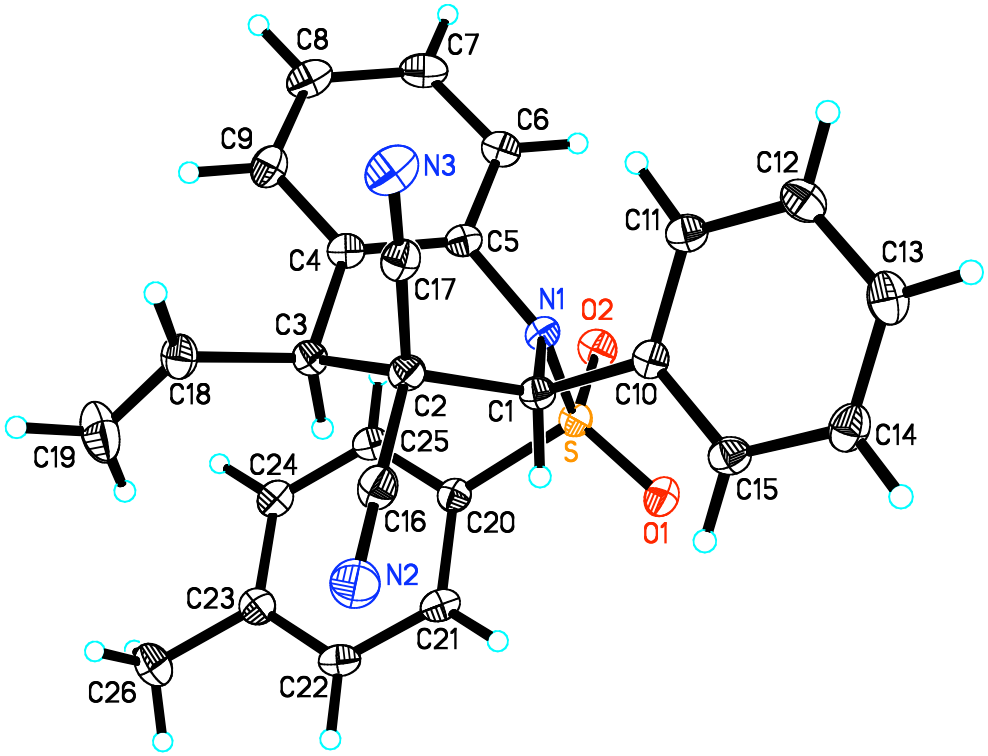
C(2)-C(3)-C(21)-C(22)	15.0(2)
C(4)-C(3)-C(21)-C(22)	-100.89(17)
C(6)-C(3)-C(21)-C(26)	-35.88(19)
C(2)-C(3)-C(21)-C(26)	-161.99(14)
C(4)-C(3)-C(21)-C(26)	82.09(17)
C(26)-C(21)-C(22)-C(23)	-0.2(3)
C(3)-C(21)-C(22)-C(23)	-177.29(16)
C(21)-C(22)-C(23)-C(24)	0.2(3)
C(22)-C(23)-C(24)-C(25)	-0.4(3)
C(23)-C(24)-C(25)-C(26)	0.6(3)
C(24)-C(25)-C(26)-C(21)	-0.7(3)
C(22)-C(21)-C(26)-C(25)	0.4(2)
C(3)-C(21)-C(26)-C(25)	177.59(14)
O(1)-S-C(31)-C(32)	-23.44(15)
O(2)-S-C(31)-C(32)	-154.76(12)
N(1)-S-C(31)-C(32)	92.84(14)
O(1)-S-C(31)-C(36)	160.70(12)
O(2)-S-C(31)-C(36)	29.39(15)
N(1)-S-C(31)-C(36)	-83.02(14)
C(36)-C(31)-C(32)-C(33)	0.3(2)
S-C(31)-C(32)-C(33)	-175.49(13)
C(31)-C(32)-C(33)-C(34)	1.8(3)
C(32)-C(33)-C(34)-C(35)	-2.1(3)
C(32)-C(33)-C(34)-C(37)	178.02(17)
C(33)-C(34)-C(35)-C(36)	0.2(2)
C(37)-C(34)-C(35)-C(36)	-179.90(16)
C(34)-C(35)-C(36)-C(31)	1.9(2)
C(32)-C(31)-C(36)-C(35)	-2.2(2)
S-C(31)-C(36)-C(35)	173.67(12)

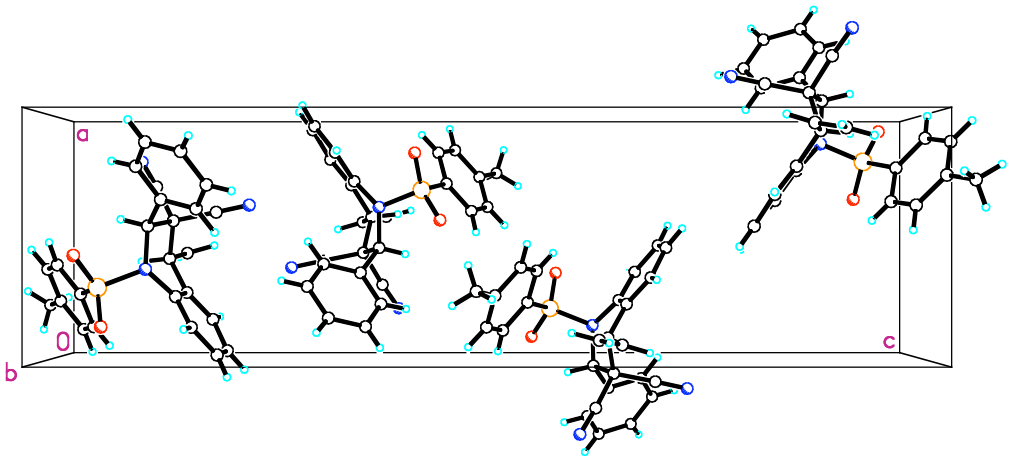


33a (cw3194)

33a was synthesized by the standard asymmetric decarboxylative cycloaddition reaction from benzoxazinanone. The colorless crystal was formed in ethanol.

Crystal Structure Data:





Comments

The asymmetric unit contains one $C_{26}H_{21}N_3O_2S$ molecule. All displacement ellipsoids are drawn at the 50% probability level.

Brief Experimental Description to be Included as Text or as a Footnote at Time of Publication

Colorless crystals of $C_{26}H_{21}N_3O_2S$ are, at 100(2) K, orthorhombic, space group $P2_12_12_1 - D_2^4$ (No. 19)[2] with **a** = 8.4257(6) Å, **b** = 8.7925(6) Å, **c** = 30.075(2) Å, V = 2228.1(3) $Å^3$ and Z = 4 molecules {d_{calcd} = 1.310 g/cm^3; μ_a(MoKα) = 0.174 mm^{-1}}. A full hemisphere of diffracted intensities (1850 10-second frames with a ω scan width of 0.30°) was measured for a single-domain specimen using graphite-monochromated MoKα radiation (λ= 0.71073 Å) on a Bruker SMART APEX CCD Single Crystal Diffraction System.[3] X-rays were provided by a fine-focus sealed x-ray tube operated at 50kV and 30mA. Lattice constants were determined with the Bruker SAINT software package using peak centers for 9106 reflections. A total of 26648 integrated reflection intensities having 2θ((MoKα) < 60.07° were produced using the Bruker program SAINT;[4] 6483 of these were unique and gave R_{int} = 0.044 with a coverage which was 99.8% complete. The data were corrected empirically for variable absorption effects using equivalent reflections; the relative transmission

factors ranged from 0.902 to 1.000. The Bruker software package SHELXTL was used to solve the structure using "direct methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted using F_o^2 data with the SHELXTL Version 6.10 software package.[5]

The final structural model incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. All hydrogen atoms were located in a difference Fourier and included in the structural model as independent isotropic atoms whose parameters were allowed to vary in least-squares refinement cycles. A total of 373 parameters were refined using no restraints, 6483 data and weights of $w = 1/ [\sigma^2(F^2) + (0.0545\ P)^2]$, where $P = [F_o^2 + 2F_c^2] / 3$. Final agreement factors at convergence are: R_1(unweighted, based on F) = 0.042 for 6087 independent absorption-corrected "observed" reflections having $2\theta(MoK\alpha) < 60.07°$ and $I > 2\sigma(I)$; R_1(unweighted, based on F) = 0.045 and wR_2(weighted, based on F^2) = 0.094 for all 6483 independent absorption-corrected reflections having $2\theta(MoK\alpha) < 60.07°$. The largest shift/s.u. was 0.000 in the final refinement cycle. The final difference map had maxima and minima of 0.47 and -0.25 $e^-/Å^3$, respectively. The absolute configuration for the $C_{26}H_{21}N_3O_2S$ molecule was reliably determined experimentally using anomalous dispersion of the x-rays; the "Flack" absolute structure parameter refined to a final value of 0.02(5).

Acknowledgment

The authors thank the National Science Foundation (grant CHE-0079282) and the University of Kansas for funds to purchase the x-ray instrument and computers.

Table 1. Crystal data and structure refinement for $C_{26}H_{21}N_3O_2S$.

Empirical formula	$C_{26}H_{21}N_3O_2S$	
Formula weight	439.52	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1 - D_2^4$ (No. 19)	
Unit cell dimensions	**a** = 8.4257(6) Å	α = 90.000°
	b = 8.7925(6) Å	β = 90.000°
	c = 30.075(2) Å	γ = 90.000°
Volume	2228.1(3) $Å^3$	
Z	4	
Density (calculated)	1.310 Mg/m^3	
Absorption coefficient	0.174 mm^{-1}	
F(000)	920	
Crystal size	0.42 x 0.24 x 0.12 mm^3	
Theta range for data collection	2.41° to 30.03°	
Index ranges	$-11 \le h \le 11$, $-12 \le k \le 12$, $-42 \le l \le 41$	
Reflections collected	26648	
Independent reflections	6483 [R_{int} = 0.044]	
Completeness to theta = 30.03°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.902	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6483 / 0 / 373	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R_1 = 0.042, wR_2 = 0.092	
R indices (all data)	R_1 = 0.045, wR_2 = 0.094	
Absolute structure parameter	0.02(5)	
Largest diff. peak and hole	0.47 and -0.25 $e^-/Å^3$	

$R_1 = \Sigma \, ||F_o| - |F_c|| \, / \, \Sigma \, |F_o|$

$wR_2 = \{ \, \Sigma \, [w(F_o^2 - F_c^2)^2] \, / \, \Sigma \, [w(F_o^2)^2] \, \}^{1/2}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for $C_{26}H_{21}N_3O_2S$. U (eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
S	6959(1)	3949(1)	4246(1)	15(1)
O(1)	5703(1)	4755(1)	4462(1)	20(1)
O(2)	8462(1)	4661(1)	4171(1)	21(1)
N(1)	6253(1)	3479(1)	3744(1)	14(1)
N(2)	1931(2)	131(2)	3935(1)	30(1)
N(3)	3709(2)	1414(2)	2672(1)	26(1)
C(1)	4559(2)	3011(2)	3740(1)	14(1)
C(2)	4341(2)	1380(2)	3526(1)	16(1)
C(3)	5870(2)	391(2)	3609(1)	15(1)
C(4)	7227(2)	1193(2)	3380(1)	15(1)
C(5)	7347(2)	2762(2)	3443(1)	15(1)
C(6)	8525(2)	3606(2)	3237(1)	18(1)
C(7)	9653(2)	2864(2)	2979(1)	21(1)
C(8)	9568(2)	1299(2)	2922(1)	22(1)
C(9)	8340(2)	468(2)	3115(1)	20(1)
C(10)	3535(2)	4249(2)	3542(1)	15(1)
C(11)	3904(2)	4909(2)	3132(1)	17(1)
C(12)	3012(2)	6121(2)	2974(1)	20(1)
C(13)	1761(2)	6697(2)	3224(1)	22(1)
C(14)	1388(2)	6043(2)	3630(1)	21(1)
C(15)	2265(2)	4820(2)	3787(1)	18(1)
C(16)	2959(2)	670(2)	3745(1)	20(1)
C(17)	3995(2)	1426(2)	3043(1)	17(1)

C(18)	5659(2)	-1241(2)	3474(1)	20(1)
C(19)	5901(3)	-2365(2)	3750(1)	34(1)
C(20)	7264(2)	2223(2)	4523(1)	16(1)
C(21)	6112(2)	1681(2)	4814(1)	18(1)
C(22)	6308(2)	249(2)	5005(1)	20(1)
C(23)	7627(2)	-641(2)	4908(1)	19(1)
C(24)	8770(2)	-74(2)	4614(1)	19(1)
C(25)	8603(2)	1348(2)	4422(1)	17(1)
C(26)	7843(2)	-2181(2)	5118(1)	26(1)

Table 3. Bond lengths [Å] for $C_{26}H_{21}N_3O_2S$.

S-O(2)	1.430(1)	C(6)-H(6)	0.94(2)
S-O(1)	1.430(1)	C(7)-C(8)	1.389(3)
S-N(1)	1.674(1)	C(7)-H(7)	0.94(2)
S-C(20)	1.751(2)	C(8)-C(9)	1.393(2)
N(1)-C(5)	1.438(2)	C(8)-H(8)	0.96(2)
N(1)-C(1)	1.486(2)	C(9)-H(9)	0.93(2)
N(2)-C(16)	1.140(2)	C(10)-C(15)	1.393(2)
N(3)-C(17)	1.142(2)	C(10)-C(11)	1.399(2)
C(1)-C(10)	1.511(2)	C(11)-C(12)	1.387(2)
C(1)-C(2)	1.582(2)	C(11)-H(11)	1.00(2)
C(1)-H(1)	0.95(2)	C(12)-C(13)	1.391(2)
C(2)-C(16)	1.477(2)	C(12)-H(12)	0.94(2)
C(2)-C(17)	1.483(2)	C(13)-C(14)	1.383(2)
C(2)-C(3)	1.574(2)	C(13)-H(13)	0.92(2)
C(3)-C(18)	1.502(2)	C(14)-C(15)	1.388(2)
C(3)-C(4)	1.509(2)	C(14)-H(14)	0.91(2)
C(3)-H(3)	0.96(2)	C(15)-H(15)	0.95(2)
C(4)-C(9)	1.387(2)	C(18)-C(19)	1.306(2)
C(4)-C(5)	1.396(2)	C(18)-H(18)	0.97(2)
C(5)-C(6)	1.386(2)	C(19)-H(19A)	0.93(2)
C(6)-C(7)	1.389(2)	C(19)-H(19B)	0.96(3)

C(20)-C(21)	1.392(2)	C(23)-C(26)	1.504(2)
C(20)-C(25)	1.399(2)	C(24)-C(25)	1.384(2)
C(21)-C(22)	1.394(2)	C(24)-H(24)	1.00(2)
C(21)-H(21)	0.93(2)	C(25)-H(25)	0.90(2)
C(22)-C(23)	1.390(2)	C(26)-H(26A)	0.94(3)
C(22)-H(22)	0.96(2)	C(26)-H(26B)	0.88(3)
C(23)-C(24)	1.400(2)	C(26)-H(26C)	0.93(3)

Table 4. Bond angles [°] for $C_{26}H_{21}N_3O_2S$.

O(2)-S-O(1)	120.6(1)	C(4)-C(3)-C(2)	106.9(1)
O(2)-S-N(1)	106.4(1)	C(18)-C(3)-H(3)	109(1)
O(1)-S-N(1)	105.7(1)	C(4)-C(3)-H(3)	111(1)
O(2)-S-C(20)	108.9(1)	C(2)-C(3)-H(3)	103(1)
O(1)-S-C(20)	108.7(1)	C(9)-C(4)-C(5)	118.9(1)
N(1)-S-C(20)	105.5(1)	C(9)-C(4)-C(3)	124.1(1)
C(5)-N(1)-C(1)	119.3(1)	C(5)-C(4)-C(3)	117.1(1)
C(5)-N(1)-S	116.6(1)	C(6)-C(5)-C(4)	121.4(1)
C(1)-N(1)-S	114.7(1)	C(6)-C(5)-N(1)	120.4(1)
N(1)-C(1)-C(10)	110.7(1)	C(4)-C(5)-N(1)	118.2(1)
N(1)-C(1)-C(2)	111.5(1)	C(5)-C(6)-C(7)	119.2(2)
C(10)-C(1)-C(2)	115.3(1)	C(5)-C(6)-H(6)	120(1)
N(1)-C(1)-H(1)	105(1)	C(7)-C(6)-H(6)	121(1)
C(10)-C(1)-H(1)	109(1)	C(6)-C(7)-C(8)	120.0(2)
C(2)-C(1)-H(1)	105(1)	C(6)-C(7)-H(7)	120(1)
C(16)-C(2)-C(17)	107.1(1)	C(8)-C(7)-H(7)	120(1)
C(16)-C(2)-C(3)	110.0(1)	C(7)-C(8)-C(9)	120.4(2)
C(17)-C(2)-C(3)	109.3(1)	C(7)-C(8)-H(8)	119(1)
C(16)-C(2)-C(1)	107.0(1)	C(9)-C(8)-H(8)	121(1)
C(17)-C(2)-C(1)	113.3(1)	C(4)-C(9)-C(8)	120.1(2)
C(3)-C(2)-C(1)	110.0(1)	C(4)-C(9)-H(9)	119(1)
C(18)-C(3)-C(4)	114.5(1)	C(8)-C(9)-H(9)	121(1)
C(18)-C(3)-C(2)	112.9(1)	C(15)-C(10)-C(11)	119.2(1)

C(15)-C(10)-C(1)	119.4(1)	C(21)-C(20)-C(25)	120.7(1)
C(11)-C(10)-C(1)	121.3(1)	C(21)-C(20)-S	119.6(1)
C(12)-C(11)-C(10)	119.9(2)	C(25)-C(20)-S	119.5(1)
C(12)-C(11)-H(11)	117(1)	C(20)-C(21)-C(22)	119.1(2)
C(10)-C(11)-H(11)	123(1)	C(20)-C(21)-H(21)	120(1)
C(11)-C(12)-C(13)	120.4(1)	C(22)-C(21)-H(21)	121(1)
C(11)-C(12)-H(12)	119(1)	C(23)-C(22)-C(21)	121.1(2)
C(13)-C(12)-H(12)	120(1)	C(23)-C(22)-H(22)	121(1)
C(14)-C(13)-C(12)	119.8(2)	C(21)-C(22)-H(22)	118(1)
C(14)-C(13)-H(13)	123(1)	C(22)-C(23)-C(24)	118.8(2)
C(12)-C(13)-H(13)	117(1)	C(22)-C(23)-C(26)	121.0(2)
C(13)-C(14)-C(15)	120.1(2)	C(24)-C(23)-C(26)	120.2(2)
C(13)-C(14)-H(14)	123(1)	C(25)-C(24)-C(23)	121.0(2)
C(15)-C(14)-H(14)	118(1)	C(25)-C(24)-H(24)	120(1)
C(14)-C(15)-C(10)	120.5(1)	C(23)-C(24)-H(24)	119(1)
C(14)-C(15)-H(15)	121(1)	C(24)-C(25)-C(20)	119.3(2)
C(10)-C(15)-H(15)	119(1)	C(24)-C(25)-H(25)	119(1)
N(2)-C(16)-C(2)	176.6(2)	C(20)-C(25)-H(25)	122(1)
N(3)-C(17)-C(2)	177.7(2)	C(23)-C(26)-H(26A)	111(2)
C(19)-C(18)-C(3)	122.2(2)	C(23)-C(26)-H(26B)	114(2)
C(19)-C(18)-H(18)	122(1)	H(26A)-C(26)-H(26B)	107(3)
C(3)-C(18)-H(18)	116(1)	C(23)-C(26)-H(26C)	114(2)
C(18)-C(19)-H(19A)	122(1)	H(26A)-C(26)-H(26C)	103(2)
C(18)-C(19)-H(19B)	121(2)	H(26B)-C(26)-H(26C)	107(3)
H(19A)-C(19)-H(19B)	117(2)		

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{26}H_{21}N_3O_2S$. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U_{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U_{12}\ ]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S	15(1)	16(1)	15(1)	-2(1)	-2(1)	-1(1)

O(1)	22(1)	19(1)	21(1)	-3(1)	0(1)	2(1)
O(2)	20(1)	21(1)	21(1)	-1(1)	-3(1)	-5(1)
N(1)	12(1)	16(1)	14(1)	-2(1)	-1(1)	-2(1)
N(2)	24(1)	26(1)	40(1)	-1(1)	10(1)	-4(1)
N(3)	20(1)	33(1)	25(1)	-5(1)	-1(1)	1(1)
C(1)	13(1)	16(1)	14(1)	0(1)	0(1)	-2(1)
C(2)	13(1)	16(1)	17(1)	-1(1)	1(1)	-2(1)
C(3)	14(1)	16(1)	17(1)	1(1)	0(1)	-1(1)
C(4)	12(1)	19(1)	16(1)	0(1)	-2(1)	-1(1)
C(5)	12(1)	20(1)	13(1)	0(1)	-2(1)	1(1)
C(6)	15(1)	21(1)	17(1)	1(1)	-2(1)	-3(1)
C(7)	13(1)	33(1)	18(1)	2(1)	0(1)	-5(1)
C(8)	14(1)	33(1)	19(1)	-4(1)	-1(1)	2(1)
C(9)	16(1)	21(1)	22(1)	-3(1)	-3(1)	3(1)
C(10)	13(1)	15(1)	17(1)	-1(1)	-1(1)	-1(1)
C(11)	15(1)	20(1)	17(1)	-1(1)	1(1)	-2(1)
C(12)	18(1)	22(1)	21(1)	4(1)	-3(1)	-2(1)
C(13)	18(1)	19(1)	29(1)	1(1)	-6(1)	0(1)
C(14)	15(1)	21(1)	28(1)	-3(1)	1(1)	1(1)
C(15)	14(1)	20(1)	19(1)	-1(1)	2(1)	-3(1)
C(16)	17(1)	19(1)	24(1)	-3(1)	1(1)	-1(1)
C(17)	11(1)	18(1)	22(1)	-2(1)	1(1)	0(1)
C(18)	19(1)	17(1)	24(1)	-3(1)	-2(1)	-2(1)
C(19)	45(1)	18(1)	38(1)	1(1)	-13(1)	-4(1)
C(20)	16(1)	17(1)	14(1)	-1(1)	-3(1)	0(1)
C(21)	16(1)	24(1)	15(1)	-1(1)	1(1)	1(1)
C(22)	20(1)	26(1)	15(1)	0(1)	2(1)	-2(1)
C(23)	20(1)	20(1)	16(1)	-1(1)	-4(1)	-2(1)
C(24)	15(1)	22(1)	19(1)	-3(1)	-3(1)	2(1)
C(25)	14(1)	21(1)	17(1)	-1(1)	-1(1)	-1(1)
C(26)	28(1)	21(1)	30(1)	5(1)	-2(1)	0(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{26}H_{21}N_3O_2S$.

	x	y	z	U(eq)
H(1)	4294(19)	2884(19)	4043(5)	7(4)
H(3)	5990(20)	435(19)	3925(6)	11(4)
H(6)	8560(20)	4670(20)	3275(6)	22(5)
H(7)	10490(20)	3420(20)	2851(6)	24(5)
H(8)	10360(20)	800(20)	2747(6)	19(5)
H(9)	8270(20)	-580(20)	3073(6)	21(5)
H(11)	4820(20)	4580(20)	2944(6)	16(4)
H(12)	3250(20)	6550(20)	2695(6)	24(5)
H(13)	1220(20)	7510(20)	3110(6)	17(4)
H(14)	550(20)	6360(20)	3796(6)	17(4)
H(15)	2040(20)	4380(20)	4069(7)	26(5)
H(18)	5340(20)	-1420(20)	3169(6)	13(4)
H(19A)	5850(20)	-3370(20)	3658(6)	27(5)
H(19B)	6180(30)	-2180(30)	4054(8)	51(7)
H(21)	5210(30)	2260(30)	4871(6)	31(5)
H(22)	5520(20)	-100(20)	5213(6)	29(5)
H(24)	9720(20)	-710(20)	4546(6)	18(5)
H(25)	9340(20)	1680(20)	4228(7)	29(5)
H(26A)	7270(40)	-2260(40)	5386(10)	81(10)
H(26B)	7540(40)	-2940(40)	4948(11)	73(9)
H(26C)	8880(40)	-2380(40)	5207(9)	77(10)

Table 7. Torsion angles [°] for $C_{26}H_{21}N_3O_2S$.

O(2)-S-N(1)-C(5)	45.5(1)
O(1)-S-N(1)-C(5)	174.9(1)
C(20)-S-N(1)-C(5)	-70.1(1)
O(2)-S-N(1)-C(1)	-168.1(1)
O(1)-S-N(1)-C(1)	-38.7(1)
C(20)-S-N(1)-C(1)	76.3(1)
C(5)-N(1)-C(1)-C(10)	-108.7(1)
S-N(1)-C(1)-C(10)	105.9(1)
C(5)-N(1)-C(1)-C(2)	21.0(2)
S-N(1)-C(1)-C(2)	-124.4(1)
N(1)-C(1)-C(2)-C(16)	149.1(1)
C(10)-C(1)-C(2)-C(16)	-83.7(2)
N(1)-C(1)-C(2)-C(17)	-93.0(2)
C(10)-C(1)-C(2)-C(17)	34.2(2)
N(1)-C(1)-C(2)-C(3)	29.7(2)
C(10)-C(1)-C(2)-C(3)	156.9(1)
C(16)-C(2)-C(3)-C(18)	54.0(2)
C(17)-C(2)-C(3)-C(18)	-63.4(2)
C(1)-C(2)-C(3)-C(18)	171.6(1)
C(16)-C(2)-C(3)-C(4)	-179.4(1)
C(17)-C(2)-C(3)-C(4)	63.3(2)
C(1)-C(2)-C(3)-C(4)	-61.7(1)
C(18)-C(3)-C(4)-C(9)	-8.6(2)
C(2)-C(3)-C(4)-C(9)	-134.3(1)
C(18)-C(3)-C(4)-C(5)	171.2(1)
C(2)-C(3)-C(4)-C(5)	45.5(2)
C(9)-C(4)-C(5)-C(6)	1.6(2)
C(3)-C(4)-C(5)-C(6)	-178.1(1)
C(9)-C(4)-C(5)-N(1)	-175.7(1)
C(3)-C(4)-C(5)-N(1)	4.6(2)
C(1)-N(1)-C(5)-C(6)	141.1(1)
S-N(1)-C(5)-C(6)	-74.1(2)

C(1)-N(1)-C(5)-C(4)	-41.6(2)
S-N(1)-C(5)-C(4)	103.2(1)
C(4)-C(5)-C(6)-C(7)	-3.0(2)
N(1)-C(5)-C(6)-C(7)	174.3(1)
C(5)-C(6)-C(7)-C(8)	1.6(2)
C(6)-C(7)-C(8)-C(9)	1.1(2)
C(5)-C(4)-C(9)-C(8)	1.1(2)
C(3)-C(4)-C(9)-C(8)	-179.2(1)
C(7)-C(8)-C(9)-C(4)	-2.5(2)
N(1)-C(1)-C(10)-C(15)	-124.4(1)
C(2)-C(1)-C(10)-C(15)	108.0(2)
N(1)-C(1)-C(10)-C(11)	50.9(2)
C(2)-C(1)-C(10)-C(11)	-76.7(2)
C(15)-C(10)-C(11)-C(12)	0.2(2)
C(1)-C(10)-C(11)-C(12)	-175.1(1)
C(10)-C(11)-C(12)-C(13)	0.7(2)
C(11)-C(12)-C(13)-C(14)	-1.0(2)
C(12)-C(13)-C(14)-C(15)	0.3(2)
C(13)-C(14)-C(15)-C(10)	0.6(2)
C(11)-C(10)-C(15)-C(14)	-0.9(2)
C(1)-C(10)-C(15)-C(14)	174.5(1)
C(17)-C(2)-C(16)-N(2)	180(100)
C(3)-C(2)-C(16)-N(2)	61(3)
C(1)-C(2)-C(16)-N(2)	-59(3)
C(16)-C(2)-C(17)-N(3)	-43(4)
C(3)-C(2)-C(17)-N(3)	77(4)
C(1)-C(2)-C(17)-N(3)	-160(4)
C(4)-C(3)-C(18)-C(19)	113.2(2)
C(2)-C(3)-C(18)-C(19)	-124.3(2)
O(2)-S-C(20)-C(21)	149.1(1)
O(1)-S-C(20)-C(21)	15.9(1)
N(1)-S-C(20)-C(21)	-97.1(1)
O(2)-S-C(20)-C(25)	-36.0(1)
O(1)-S-C(20)-C(25)	-169.2(1)

N(1)-S-C(20)-C(25)	77.9(1)
C(25)-C(20)-C(21)-C(22)	-0.1(2)
S-C(20)-C(21)-C(22)	174.8(1)
C(20)-C(21)-C(22)-C(23)	-0.2(2)
C(21)-C(22)-C(23)-C(24)	0.1(2)
C(21)-C(22)-C(23)-C(26)	179.4(2)
C(22)-C(23)-C(24)-C(25)	0.2(2)
C(26)-C(23)-C(24)-C(25)	-179.1(2)
C(23)-C(24)-C(25)-C(20)	-0.5(2)
C(21)-C(20)-C(25)-C(24)	0.4(2)
S-C(20)-C(25)-C(24)	-174.5(1)

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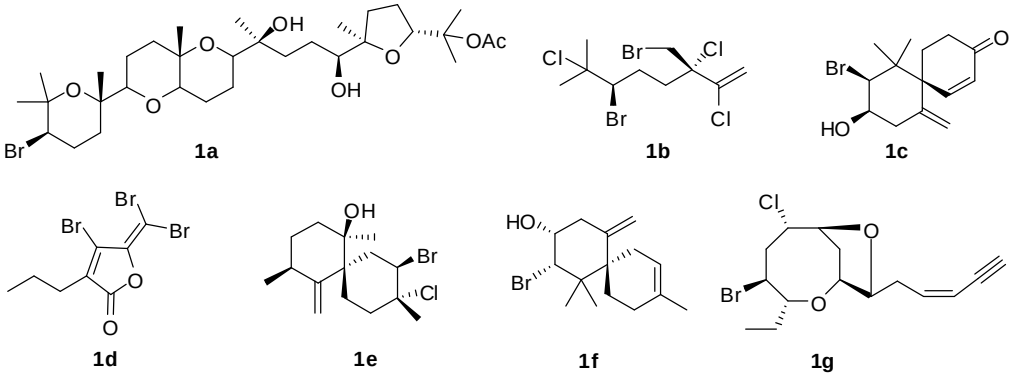
Chapter 4

Selenocatalytic α-Halogenation

4.1 Importance of Catalytic *α*-Halogenation of Carbonyl Compounds

Halogenation reactions have drawn a lot of attention and been extensively studied. The reason partially resides in the fact that a large amount of halogenated natural products, isolated from terrestrial and marine organisms displayed interesting biological and pharmaceutical activities as shown in Scheme 1. For instance, thyrsiferyl acetate **1a** is known to inhibit protein phosphatase and halomon **1b** displays antitumor and cytotoxic activities.[1-3] Mailione **1c** showed interesting anthelminthic properties and furanones **1d** exhibits anti-fouling properties.[4-6] Cyclized sesquiterpenes **1e, 1f** and acetogenins **1g** display broad spectrum antimicrobial and antiviral activity.[7] Halogens are known to be the bioisosteres of a wide variety of atoms such as hydrogen and carbon.[8] Introducing halogens into the drug candidate can potentially enhance both the activity and bioavailability, for example chlorination improves the lipophilicity of the medicine.

Scheme 1 *Halogenated marine natural products*

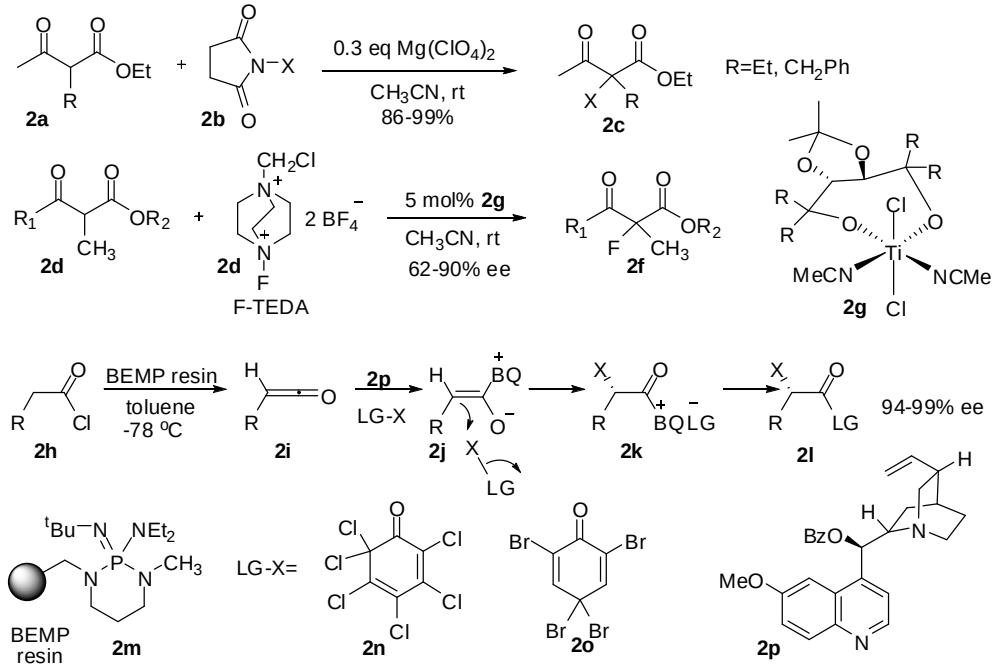


Secondly, halogenated products are important synthetic intermediates for further manipulations, and this trend has been further magnified by those discoveries of transition metal-catalyzed coupling reactions such as Suzuki, Stille, Heck, Sonogashira etc.[9-12]

Traditionally, α-halogenation of carbonyl compounds uses reagents such as HOX or X_2, which often exhibit poor chemoselectivity and competing side reactions such as dihalogenation.[13, 14] Catalytic α-halogenation has been introduced into this scenario to address such a problem and received much attention lately due to the importance of the products as synthetic precursors and pharmaceuticals.[15] The majority of these methods focus on the catalytic activation of the carbonyl substrate by formation of enolates as shown in Scheme 2. α-Halogenations of β-ketoesters **2a** with *N*-halosuccinimide were carried out under mild conditions in the presence of a Lewis acid catalyst $Mg(ClO_4)_2$.[16] Enantiomerically enriched products **2f** were produced in 62-90% ee by treatment of β-ketoesters **2d** with a fluorination reagent **2d** catalyzed by a chiral Lewis acid complex **2g**.[17] Lectka *et al.* reported a novel catalyst system for asymmetric chlorination and bromination. A chiral benzoylquinine catalyst functioned as a nucleophile to react with ketenes **2i** to give acylammonium enolates, which were then halogenated to generate products **2k** in decent yield and excellent eantioselectivities.[18] However, those transformations have drawbacks in terms of

substrate scope and reaction yield. For example, in the first two cases, the α-substituents of β-ketoesters **2a** and **2d** are necessary in order to avoid the formation of dihalogenated products. The yields of the third reaction were hampered by a homodimerization side reactions.

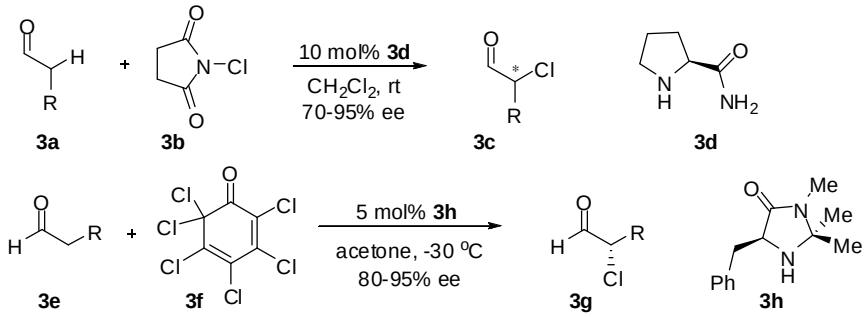
Scheme 2 *Catalytic α-halogenation via enolate intermediates*



Catalytic activation of the carbonyl substrate by formation of enamines is shown in Scheme 3. Enantiopure amines **3d** and **3h** were used to catalyze the formation of enamine intermediates, followed by chlorination to generate products **3c** and **3g** in good eantioselectivities.[8, 19] Alternatively, the catalytic formation of X_2 (X = Cl, Br, I) from H_2O_2/NaX,[20] or *N*-halosuccinimides has been a successful approach.[21] However,

in order to control the selectivity of halogenation, one would like to utilize a catalyst that halogenates ketones through reagent-bound halogens rather than freely diffusing oxidized halogen species.

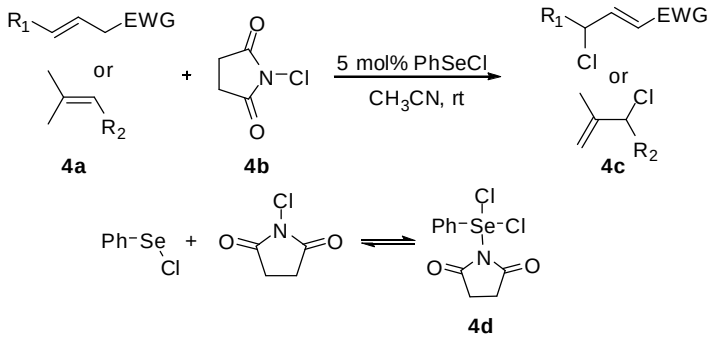
Scheme 3 *Catalytic α-halogenation via enamine intermediates*



4.2 Selenium-Catalyzed Halogenation of Carbonyl Compounds

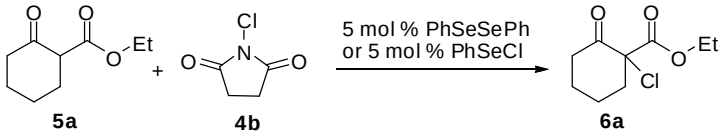
Recently, we described the use of phenylselenium chloride as a catalyst for allylic halogenation of olefins with *N*-chlorosuccinimide (NCS) **4b** as shown in Scheme 4.[22] In the course of these studies we noted that the reaction was inhibited by NCS. To explain the observed inhibition we postulated that the phenylselenyl chloride catalyst was in equilibrium with the oxidized PhSe(succinimide)Cl_2 **4d**.[23] While PhSe(succinimide)Cl_2 **4d** was less active for allylic halogenation, it is known that the related $PhSeCl_3$ α-halogenates ketones.[24] Therefore we thought that **4d** might be a useful catalyst for the α-halogenation of ketones with NCS.

Scheme 4 *Selenocatalytic allylic chlorinations*



In order to test whether arylselenides can activate NCS toward nucleophilic attack, 2-carboxethoxycyclohexanone **5a** was treated with 5 mol% PhSeCl and 1.1 equiv. NCS in CH_3CN (Scheme 5). Analysis of the reaction mixture after 10 min. at room temperature showed complete conversion to the α-chloro product **6a**. A control reaction run in the absence of PhSeCl showed < 1% reaction.

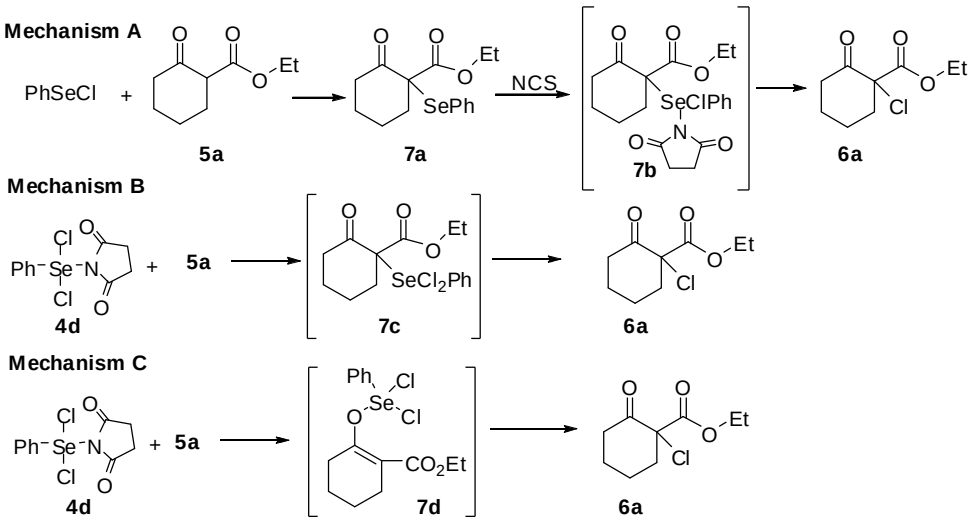
Scheme 5 *Catalytic α–chlorination of a β-ketoester*



We envisioned several possible mechanisms for product formation as shown in Scheme 6. First, the β-ketoester could be α-selenylated by PhSeCl to afford **7a**.[25, 26] Oxidation of **7a** by NCS would give **7b** which could reductively eliminate the halogenated product (Mechanism A).[27] Alternatively, the β-ketoester can be α-selenylated by the Se(IV) reagent **4d**, providing **7c**, which could liberate **6a** upon

reductive elimination (Mechanism B). Finally, selenation at oxygen would form **7d**, which could undergo intramolecular nucleophilic attack at the chlorine (Mechanism C). While mechanisms A and B differ by the oxidation state of the selenylating agent, the latter two mechanisms differ only by whether the α-carbon is electrophilically selenylated or chlorinated.

Scheme 6 *Three possible mechanisms for catalytic α–halogenation of β-ketoesters*

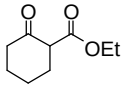
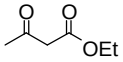
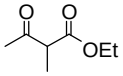
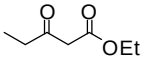
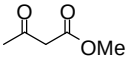
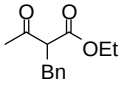
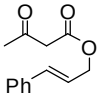


In order to gain some mechanistic insight several reactions utilizing stoichiometric PhSeCl were run. First, **5a** was treated with PhSeCl in CH_3CN. After stirring overnight, the selenylated product **7a** was isolated and purified by chromatography. Treatment of **7a** with NCS in CD_3CN at room temperature did provide halogenated product **6a**, however after standing 2.5 hours, the reaction was not complete ($t_{1/2}$ ~ 150 min.). Therefore, pathway A is not kinetically competent with

the observed catalysis ($t_{1/2}$ < 10 min.). Next, product **7a** was treated with SO_2Cl_2 in CD_3CN, which should provide intermediate **7c**.[24] Doing so led cleanly to one product, tentatively identified as **7c** based on ^1H NMR spectroscopy. This compound was stable for several hours at room temperature, but slowly decomposed overnight to give **6a** (67 % conversion after 28 h). Once again, this indicates that intermediate **7c** is not a kinetically competent intermediate. Therefore, it appears that the mechanism of catalysis is electrophilic chlorination rather that selenylation. *This is important because it shows that selenium can be used to enhance the electrophilicity of oxidized halogen sources such as NCS.*

With this knowledge in hand, we set out to explore the scope of the catalysis and the results are shown in Table 1. Halogenation of β-ketoesters provided monohalo adducts exclusively. Importantly, the halogenation could be conducted in the presence of olefins (substrate **5g**), without competing allylic halogenation.[21] Cyclohexanone **5h** was readily α-halogenated, showing that the β-keto activating group is not required. However, a qualitative correlation between the rate of the reaction and the rate of enolization is noteworthy. Unfortunately, cyclohexanone **5h** was not as selective for monochlorination, and a 4:1 mixture of α-chlorocyclohexanone: α,α'-dichloro-cyclohexane was obtained.

Table 1 *PhSeCl catalyzed α-chlorination of ketones in CH_3CN*

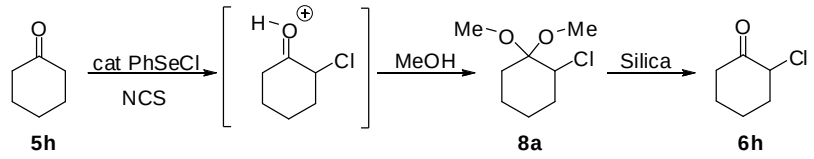
Substrate	Structure	Time	Product	Yield %
5a		10 min	6a	86
5b		10 min	6b	81
5c		18 hr	6c	63
5d		30 min	6d	74
5e		10 min	6e	68
5f		48 hr	6f	95
5g		16 hr	6g	87
5h		18 hr	6h	61[a]
5i		7 hr	6i	79[b]

[a] isolated yield of monochlorocyclohexanone [b] product is vinyl chloride.

We reasoned that the selectivity for monochlorination could be increased if the monochlorointermediate was trapped by solvent as a hemiacetal or an acetal (Scheme 7). Investigating the reaction in methanol showed that cyclohexanone was chlorinated by NCS in < 1 h at room temperature and ^{1}H and ^{13}C NMR spectroscopies of the reaction mixture showed the presence of **8a** with no evidence for dichlorinated product. α-Chlorocyclohexanone was liberated in good yield (72 %) upon passage through silica gel. Once again, no reaction occurred in the control without PhSeCl. Aside from the faster reaction kinetics in methanol, the reaction progress was

conveniently monitored by the dissolution of the relatively insoluble NCS.

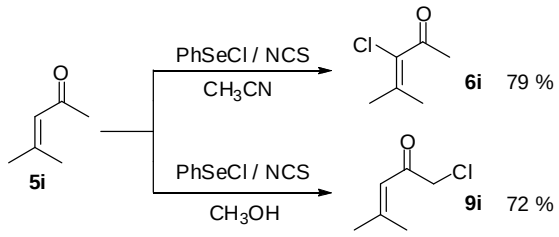
Scheme 7 *Trapping monochlorocyclohexanone in methanol*



Importantly, cyclohexanone was also α-brominated to provide α-bromocyclohexanone in 86 % yield when NBS replaced NCS. No reaction was observed in the absence of PhSeBr.

Finally, we investigated the chlorination of an α,β-unsaturated ketone, mesityl oxide **5i** (Scheme 8). Interestingly, treatment of mesityl oxide with NCS and 5 mol % PhSeCl in CH_3CN provided good yield of vinyl halide **6i**,[28] however, switching the solvent to MeOH completely reversed the selectivity and only the product of methyl halogenation **9i** was observed.

Scheme 8 *Regiochemical solvent effect*



In conclusion, we have demonstrated that phenylselenides are efficient and selective catalysts for α-chlorination of ketones. Experiments suggest that the

mechanism of the reaction involves oxidative addition of NCS to selenium which activates the “chloronium” toward nucleophilic attack by enols/enolates. This represents the first example of such an activation of oxidized halogen reagents.

4.3 References

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Appendix D

Experimental Procedures and Data for Chapter 4

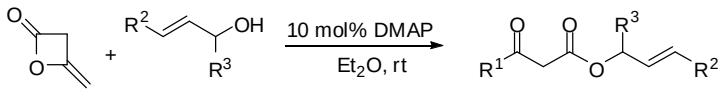
General Experimental

THF was dried over sodium metal and distilled under vacuum. Toluene, methylene chloride and diethyl ether were dried over activated alumina on a solvent system purchased from Innovative Technology, Inc.[1] Acetonitrile and 1,4-dioxane were dried and stored over activated molecular sieves. Commercially available reagents were used without additional purification unless otherwise stated. Products were purified on silica gel from Sorbent Technologies (230x400 mesh, 60 Å porosity, pH 6.5-7.5). Ruthenium and palladium compounds were obtained from Strem. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5715-7, EMD chemicals). UV lamp (254 nm) or $KMnO_4$ stain were used for monitoring TLC plates.

^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance 400 or Bruker Avance 500 DRX spectrometer and referenced to residual protio solvent signals. Structural assignments are based on ^{1}H, ^{13}C, DEPT-135, COSY, and HMQC spectroscopies and X-ray data. High resolution mass spectrometry was performed on an AUTOSPEC-Q tandem hybrid mass spectrometer (VG Analytical Ltd, Manchester, UK). High resolution mass spectrometry was performed on a LCT Premier (Waters Corp., Milford MA) time of flight mass spectrometer. FTIR spectra were acquired on a Shimadzu FTIR-8400S spectrometer. HPLC analysis was performed on a Shimadzu SCL-10A VP instrument.

Preparation of Starting Materials

Allyl *β*-ketoesters were synthesized by the DMAP catalyzed coupling reaction between commercially available allylic alcohols with diketene, followed by purification via flash column chromatography when R^1 equals to methyl group. (SiO_2, 7:1 Hexane: Ethyl acetate).[2]



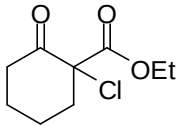
To a solution of the allylic alcohol (225 mg, 1.6 mmol) in 10 ml ether under argon was added diketene in one protion (1.8 mmol, 1.1 eq.), followed by DMAP (17.6 mg, 0.16 mmol, 0.1 eq). The reation mixture was kept stirring until reaction completion indicated by TLC (generally 1.5 hr). The reaction was quenched with sat. NH_4Cl solution, extracted with ether. The organic phase was washed with brined, dried over magnesium sulfate and concentrated to give the crude product, which was purified by flash column chromatography (SiO_2, 10:1 Hexane: Ethyl acetate). All other β-ketoesters are commercially available and used without further purification.

General procedure for Selenocatalytic *α*-Halogenation:

In a Schlenk tube under argon, PhSeCl (5 mol%, 0.13 mmol) was dissolved in 3 mL CH_3CN. To this orange color solution at room temperature was added β-ketoesters (2.51 mmol, 1.0 eq.), followed by *N*-chlorosuccinimide (2.51 mmol, 1.0 eq.). The addition resulted in an immediate color change from orange to yellow (normally in 10 mins) which indicates the reaction completion. In the mean time, the

reaction was also monitored by TLC. Following solvent evaporation the crude product was purified via flash chromatography (SiO_2, 15:1 Hexane: Ethyl acetate).

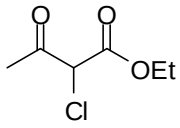
Spectroscopic Data



ethyl 1-chloro-2-oxocyclohexanecarboxylate
6a(cw1008)[3]
colorless oil
86% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (q, *J* = 7.1 Hz, 2H: OC*H*$_2$), 2.83 (m, 2H: ClCC*H*$_2$), 2.45 (m, 1H: C*H*$_2$), 2.14 (m, 1H: C*H*$_2$), 2.01-1.82 (m, 3H: C*H*$_2$), 1.75(m, 1H: C*H*$_2$), 1.31(t, *J* = 7.1 Hz, 3H: C*H*$_3$).

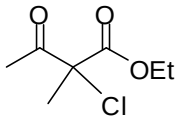
^{13}C NMR (75 MHz, $CDCl_3$) δ 199.67 (*C*=O), 167.22 (O*C*=O), 73.47 (Cl*C*), 66.82 (O*C*H$_2$), 39.60 (C=O*C*H$_2$), 38.82 (2.83) (*C*H$_2$), 26.67 (ambiguous *C*H$_2$), 22.14 (ambiguous *C*H$_2$), 13.87(*C*H$_3$).



ethyl 2-chloro-3-oxobutanoate
6b (cw1005)[4]
colorless oil
81% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.76 (s, 1H: ClC*H*), 4.30 (q, *J* = 7.1 Hz, 2H: OC*H*$_2$), 2.39 (s, 3H: C*H*$_3$C=O), 1.32 (t, *J* = 7.1 Hz, 3H: C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 199.61 (*C*=O), 164.92 (O*C*=O), 63.14 (Cl*C*), 61.31 (O*C*H$_2$), 26.21 (O=C*C*H$_3$), 13.89 (*C*H$_3$).



ethyl 2-chloro-2-methyl-3-oxobutanoate

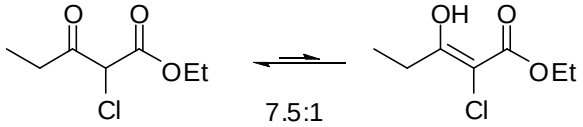
6c (cw1016)[5]

colorless oil

63% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (q, *J* = 7.1 Hz, 2H: OC*H*$_2$), 2.37 (s, 3H: C*H*$_3$C=O), 1.82 (s, 3H: C*H*$_3$CCl), 1.30 (t, *J* = 7.1 Hz, 3H: C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 198.80 (*C*=O), 168.03 (O*C*=O), 70.72 (Cl*C*), 63.04 (O*C*H$_2$), 25.25 (ambiguous *C*H$_3$), 24.22 (ambiguous *C*H$_3$), 13.89 (1.30) (*C*H$_3$).



ethyl 2-chloro-3-oxopentanoate (*E*)-ethyl 2-chloro-3-hydroxypent-2-enoate

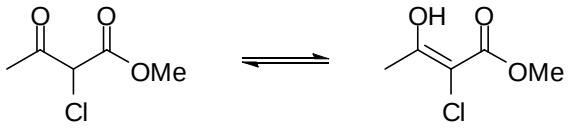
6d (cw1030)[6]

colorless oil

74% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (s, 1H: ClC*H*), 4.41 (q, *J* = 7.1 Hz, 2H: OC*H*$_2$ of the enol isomer), 4.28 (q, *J* = 7.1 Hz, 2H: OC*H*$_2$), 2.91 (q, *J* = 7.1 Hz, 2H: C*H*$_2$C=O of the enol isomer), 2.79 (q, *J* = 7.1 Hz, 2H: C*H*$_2$C=O), 1.28 (t, *J* = 7.1 Hz, 3H: ambiguous C*H*$_3$), 1.07 (t, *J* = 7.1 Hz, 3H: ambiguous C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$) δ 200,87 (*C*=O), 166.97 (O*C*=O), 64.38 (Cl*C*), 62.79 (O*C*H$_2$), 34.25 (2.79) (*C*H$_2$), 15.18 (ambiguous *C*H$_3$), 8.90 (ambiguous *C*H$_3$).

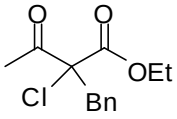


methyl 2-chloro-3-oxobutanoate (*E*)-methyl 2-chloro-3-hydroxybut-2-enoate

6e (cw1031)[7]
colorless oil
68% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.24 (1H: O*H*), 4.78 (s, 1H: C*H*Cl), 3.85 (s, 3H, ambiguous OCH_3), 3.84 (s, 3H, ambiguous OCH_3), 2.34 (s, 3H: CH_3C=O), 2.18 (s, 3H: CH_3COH).

^{13}C NMR (75 MHz, $CDCl_3$) δ 196.58 (*C*=O), 172.21 (ambiguous, O*C*=O), 169.64 (ambiguous, O*C*=O), 165.42 (HO*C*=), 96.74 (=*C*Cl), 61.06 (*C*Cl), 53.76 (ambiguous O*C*H3), 52.69 (ambiguous OCH_3), 26.27 (2.34) (*C*H_3), 19.73 (2.18) (*C*H_3).

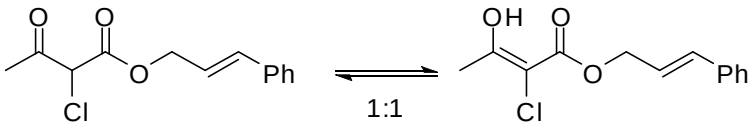


ethyl 2-benzyl-2-chloro-3-oxobutanoate

6f (cw1032)[8]
colorless oil
95% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.30 (m, 3H: arom *H*), 7.21 (m, 2H: arom *H*), 4.22 (m, 2H: OCH_2), 3.53 (dd, *J* = 14.4, 21.5 Hz, 1H: diastereotopic CH_2Ph), 3.44 (dd, *J* = 14.4, 21.5 Hz, 1H: diastereotopic CH_2Ph), 2.24 (app. d, *J* = 3.8 Hz, 3H: CH_3C=O), 1.24 (app. t, *J* = 7.1 Hz, 3H: CH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 198.90 (*C*=O), 167.02 (O*C*=O), 133.92 (arom. *C*), 130.58 (arom. *C*), 128.18 (arom. *C*), 127.48 (arom. *C*), 75.24 (Cl*C*), 63.04 (O*C*H_2), 42.15 (2.48) (*C*H_2Ph), 26.50 (2.24) (*C*H_3), 13.80 (1.24) (*C*H_3).

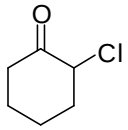


cinnamyl 2-chloro-3-oxobutanoate (*E*)-cinnamyl 2-chloro-3-hydroxybut-2-enoate

6g (cw1013)[9]
colorless oil
87% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.28 (1H: O*H*), 7.40 (m, 5H: arom *H*), 7.32 (m, 5H: arom *H*), 6.72 (dd, 2H: ambiguous C*H*=), 6.31 (m, 2H; ambiguous C*H*=), 4.89 (app. t, *J* = 4.57 Hz, 4H: ambiguous CH_2O), 4.81 (s, 1H: ClC*H*), 2.40 (s, 3H: CH_3C=O), 2.20 (s, 3H: CH_3COH).

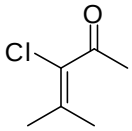
^{13}C NMR (75 MHz, $CDCl_3$) δ 207.36 (*C*=O), 143.35 (arom. *C*), 137.49 (arom. *C*), 132.76 (*C*H=), 130.39 (*C*H=), 129.13 (arom. *C*H), 128.91 (arom. *C*H), 128.06 (arom. *C*H), 127.75 (arom. *C*H), 127.12 (arom. *C*H), 126.65 (arom. *C*H), 49.82 (*C*H_2), 44.36 (*C*H), 31.20 (*C*H_3).



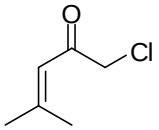
2-chlorocyclohexanone
6h (cw2056)[10]
colorless oil
61% yield

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.37 (q, *J* = 5.2 Hz, 1H: ClC*H*), 2.78 (m, 1H: diastereotopic ClCCH_2), 2.30-2.43 (m, 2H: CH_2C=O), 1.97-2.12 (m, 2H: ambiguous CH_2), 1.88-1.95 (m, 1H: ambiguous CH_2), 1.79-1.87 (m, 1H: ambiguous CH_2), 1.68-1.77 (m, 1H: ambiguous CH_2).

^{13}C NMR (75 MHz, $CDCl_3$) δ 203.41 (*C*=O), 62.87 (Cl*C*), 39.41 (C=OCH_2), 37.40 (2.78) (*C*H_2), 27.02 (ambiguous *C*H_2), 22.90 (ambiguous *C*H_2).



3-chloro-4-methylpent-3-en-2-one
6i[11]



1-chloro-4-methylpent-3-en-2-one
9i[12]

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